ASSOCIATION BETWEEN 24 HOURS URINARY SODIUM & POTASSIUM EXCRETION AND BLOOD PRESSURE

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CHENNAI

CERTIFICATE

This is to certify that this dissertation titled **"ASSOCIATION BETWEEN 24 HOURS URINARY SODIUM & POTASSIUM EXCRETION AND BLOOD PRESSURE"** submitted by **DR. C.INDUMATHI** to the faculty of General Medicine, The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree Branch I (General Medicine) is a bonafide research work carried out by her under our direct supervision and guidance.

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DECLARATION

I, **Dr. DR. C.INDUMATHI**, solemnly declare that the dissertation titled **'ASSOCIATION BETWEEN 24 HOURS URINARY SODIUM & POTASSIUM EXCRETION AND BLOOD PRESSURE'** has been prepared by me.

This is submitted to the Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree Branch I (General Medicine).

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INTRODUCTION

Hypertension is a very common disorder especially past middle age. It is not a disease in itself, but is an important risk factor for coronary, cerebral, renal and peripheral vascular disease. [1] Of all hypertensive patients, majority of cases are of essential hypertension which accounts for about 90% of total hypertensive population. [2]

Risk factors for hypertension incidence include genetic predisposition, age, sex, BMI, smoking, alcoholism and lifestyle factors. Among lifestyle factors, high dietary sodium and low potassium intakes were found to be associated with blood pressure in many studies. [3] [4]

The large Intersalt study showed that high sodium intake was directly related to blood pressure while low potassium intake was inversely and independently related to the same. [3]A positive correlation was observed between urinary Na^+/K^+molar ratio and blood pressure. [5]

Guyton states that increased blood pressure is required to maintain renal sodium excretion and sodium balance in essential hypertension. [6]

Our present study was based on Guyton's hypothesis and aimed at studying the association between 24 hour urinary sodium and potassium excretion with blood pressure.

DEFINITION &CLASSIFICATION

DEFINITION

Hypertension is arbitrarily defined as sustained systolic blood pressure of 140 mmHg or greater and a diastolic BP of 90 mmHg or greater or by virtue of the patient taking antihypertensive medications. [7]

CLASSIFICATION

Classification of Blood pressure [7] for adults aged 18 years or older

Category	Systolic BP (mmHg)	Diastolic BP(mmHg)
Normal	<120	and <80
Prehypertension	120 - 139	or 80 - 89
Stage 1 hypertension	140 - 159	or 90 - 99
Stage 2 hypertension	≥ 160	or ≥100

This classification should be based on the mean of two or more blood pressure readings at each of two or more visits after the initial screening.

When systolic BP and diastolic BP fall into different categories,the higher category should be selected to classify the individual's BP.

EPIDEMIOLOGY

Hypertension is present globally but its prevalence varies among different countries and sub populations.Worldwide more than one billion individuals have hypertension.

Data from the National Health and Nutrition Examination Survey (NHANES 1999 to 2000) showed that approximately 31.3% of adult population in United States has hypertension.

In the Indian subcontinent, there are no well co-ordinated national surveys for prevalence of hypertension. Several regional small surveys have been conducted which showed a higher prevalence in urban population.

Many hypertensive patients have a positive family history of hypertension. In most instances, the mode of inheritance is complex and polygenic. Black men and women have a twofold higher prevalence of hypertension (30%) than white men and women (15%).

According to the data from NHANES, the prevalence of hypertension increases sharply with advancing age and high BMI. The mean levels of systolic BP and diastolic BP were also found to increase as BMI increases.

Various epidemiological studies have shown that the dietary intake of salt correlates with the average BP in a population. An international epidemiological study, INTERSALT, showed a significant correlation between dietary sodium intake and median systolic BP and diastolic BP.

Some epidemiological studies have shown that low calcium and potassium intake may also lead to hypertension. Blood pressure is strongly related to urinary sodium and potassium molar ratio than either sodium or potassium alone.

Data derived from the Framingham study have shown that hypertensive patients have a fourfold increase in cerebrovascular accidents , as well as a sixfold increase in congestive heart failure when compared to normotensive subjects.

Higher the levels of systolic BP and diastolic BP, higher the disease associated morbidity and mortality which includes atherosclerotic cardiovascular disease, stroke, heart failure and renal insufficiency.

Cardiovascular and cerebrovascular mortality rates have substantially decreased in the past three decades owing to aggressive treatment of hypertension. Similar results can be achieved by long term, population wide, reduction of salt intake which reduces the prevalence of hypertension in the population.

NATURAL HISTORY OF HYPERTENSION

Perera et al[43] in 1950s observed 500 untreated hypertensive patients, 150 from before the onset of their hypertension until their death and another 350 from the uncomplicated phase until their death.

The mean survival of these patients after discovery of their hypertension was 20 years. The severity of the casually obtained BP had little prognostic value. Some patients with systolic blood pressure above 200mmHg survived for more than 35 years without any treatment.

The disease process included an uncomplicated phase lasting for about 15 years followed by a complicated phase. In the complicated phase, organ complications, largely arteriolosclerotic and atherosclerotic became apparent.

Of these complications,74% were cardiac ,42% were renal and 32% were retinal. More than half the subjects died of heart disease (principally congestive cardiac failure), 10% to 15% died of cerebral accidents , and about 10% died of renal failure.

Malignant hypertension occurred in fewer than 5% of these patients.

RISK FACTORS FOR HYPERTENSION

Hypertension is a multisystem disorder with involvement of cardiovascular, neuroendocrine and renal systems with a strong genetic component.

Blood pressure is influenced by a number of environmental , genetic and lifestyle factors as shown below:

NON-MODIFIABLE RISK FACTORS

1.ROLE OF GENETICS :

"Inherited BP" refers to the variations in BP which are determined genetically. 20% to 60% of essential hypertension is inherited while the remaining is acquired or environmental.

Various environmental and lifestyle factors have an influence on inherited BP.These include excessive salt intake, weight gain and heavy alcohol intake. These factors increase the blood pressure above the inherited BP and lead to hypertension.

The interactions between genetics and environmental factors influence sympathetic overactivity, RAAS, RKKS and endothelial factors which inturn influence sodium excretion, vascular reactivity and cardiac

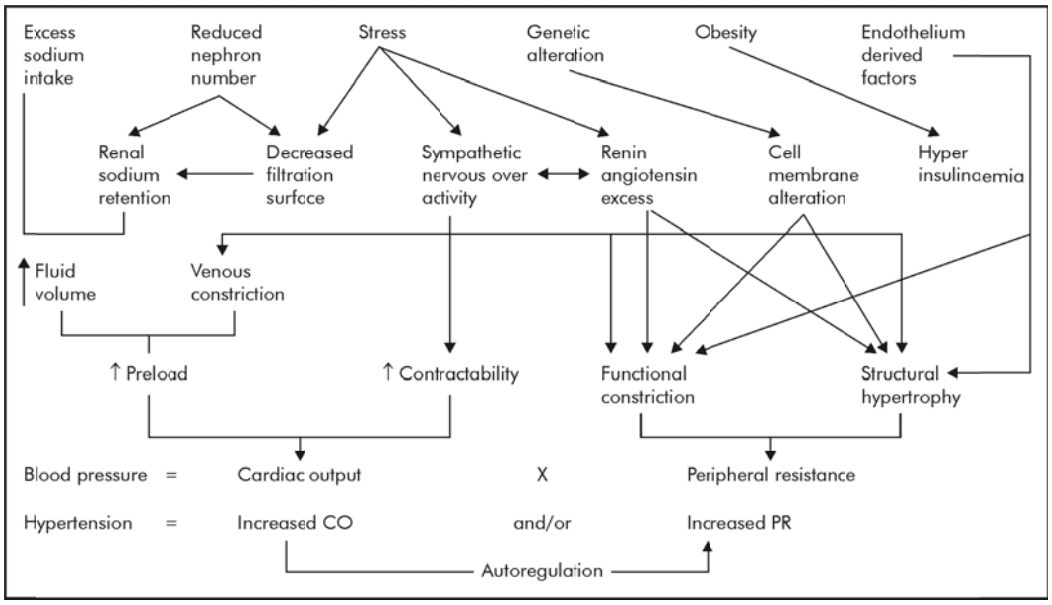
contractility. These finally determine cardiac output and peripheral vascular resistance and consequently blood pressure. Since many intermediary phenotypes are included in this complex mechanism, many genes participate in the development of hypertension.

Apart from this, genetic factors also play a role in the behavioural pattern of individuals which elevates blood pressure. So, it is difficult to assess the proportion of blood pressure variability due to inheritance and this varies in different populations.

Mutations in the genes raise or lower blood pressure by altering salt and water reabsorption by the nephron through common pathways. The genetic mutations responsible for three rare forms of mendelian hypertension syndromes – Glucocorticoid remediable aldosteronism (GRA), Liddle's syndrome and apparent mineralocorticoid excess (AME) have been identified.

Polymorphisms and mutations in the genes for angiotensin converting enzyme, angiotensin, B_2 adrenergic receptor, adducin, angiotensinase C, renin binding proteins, G protein B3 subunit, atrial natriuretic factor and the insulin receptor are found to be associated with the development of hypertension.

FIG 1. FACTORS INVOLVED IN THE REGULATION OF BP



2.AGE :

Almost all the surveys show that blood pressure increases significantly with age in both men and women. Aging has significant effect on cardiovascular and renal functions which leads to elevated blood pressure.

In CVS, aging leads to increased arterial rigidity and peripheral vascular resistance which are in concert with reduced cardiac output, baroreceptor sensitivity and $\beta_2$adrenoceptor sensitivity and ultimately results in elevation of BP.

The effects of aging on renal functions are reduced glomerular filtration rate, renal blood flow and plasma renin activity. These changes

along with increased plasma volume results in significant elevation of blood pressure.

With aging , reductions may occur in brain metabolism, nerve conduction velocity, basal metabolic rate, vital capacity and maximum breathing capacity which contributes to rise in blood pressure.

The compliance of blood vessels is reduced with aging which leads to elevated blood pressure. False elevation of BP can also occur in elderly individuals due to thickened peripheral vessels which can be identified by Osler maneuver.

3.SEX :

In adult women, blood pressure is lower than in men of comparable age. But, the rise in blood pressure is more steep thereafter and around middle age, blood pressure is about the same in both men and women.

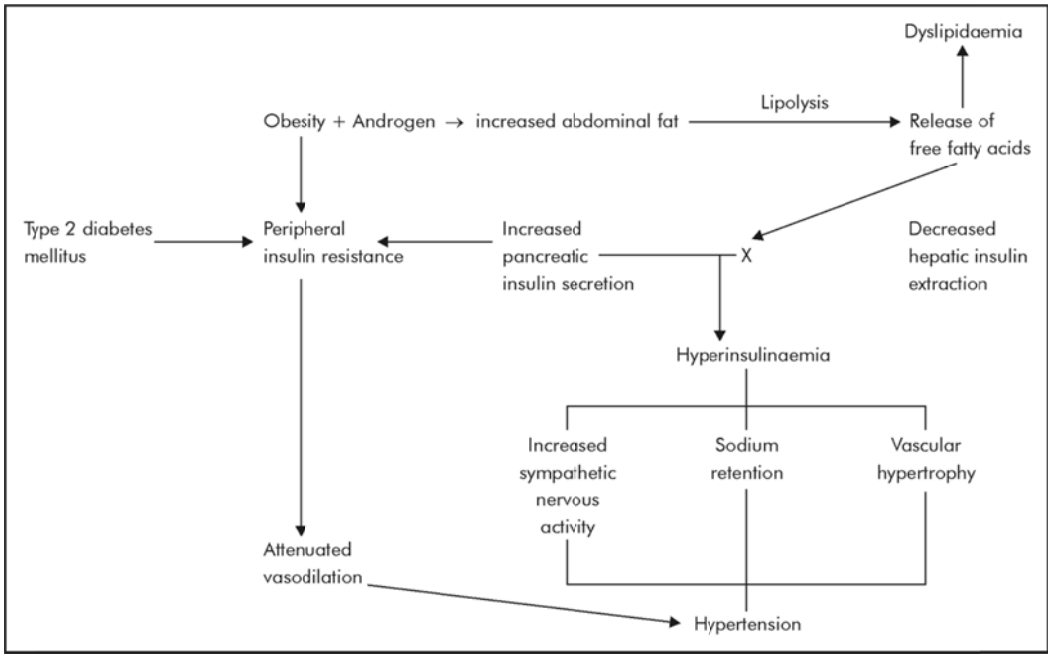
MODIFIABLE RISK FACTORS

1.OBESITY :

Obesity is one of the modifiable risk factors for the onset of hypertension. The Framingham Study showed nearly1mmHg rise of Systolic BP for every 1.25kg of weight gain.

Abdominal obesity which is evidenced by waist circumference of 80cm or more in women and 90cm or more in men has also been found to be associated with risk of hypertension. Abdominal obesity is the most dangerous risk factor. About 70% of hypertension in men and 60% in women could be attributed to abdominal obesity.

FIG 2. MECHANISMS OF OBESITY INDUCED HYPERTENSION



Cardiac output , stroke volume and total blood volume has been found to be higher while peripheral resistance is lower in obese individuals when compared to non-obese individuals. [8]

Cardiac output is directly proportional to the expansion of bodymass which is the primary reason for rise in BP. [9]The prevalence of hypertension increased equally with increasing BMI, degree of upper body obesity and fasting insulin levels. [10]

Obesity results in insulin resistance and hyperinsulinemia which are components of the metabolic syndrome. Such higher insulin levels are found to be associated with more hypertension.

Mechanisms of insulin resistance/hyperinsulinemia induced hypertension

I.Enhanced renal sodium and water absorption :

1. Increased blood pressure sensitivity to dietary salt intake.

2. Augmentation of the pressure and aldosterone responses to AII (angiotensin II).

3. Changes in transmembrane electrolyte transport

   a. Increased intracellular sodium

   b. Decreased Na^+/K^+ - ATPase activity

   c. Increased intracellular Ca^{2+} pump activity

II.Increased intracellular Ca^{2+} accumulation :

1.Stimulation of growth factors, especially in vascular smooth muscle.

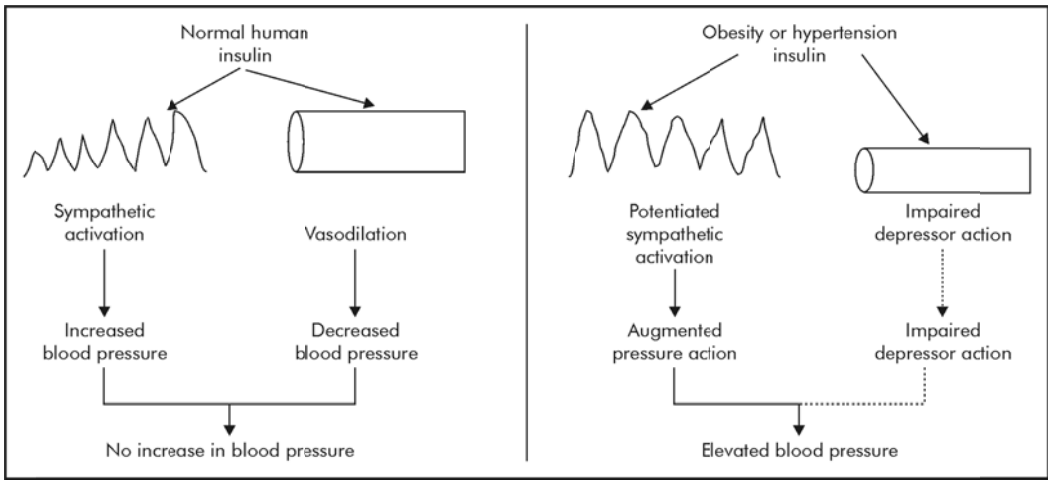
2. Stimulation of sympathetic nervous activity.

3. Reduced synthesis of vasodilatory prostaglandins.

4. Impaired vasodilation

5. Increased secretion of endothelin

FIG 3. EFFECTS OF HYPERINSULINEMIA ON BLOOD PRESSURE



Insulin increases sympathetic outflow which raises the BP and it also causes vasodilation which decreases BP, so that the net effect on BP is zero. An imbalance between these pressor and depressor actions of insulin in conditions such as obesity leads to elevated blood pressure. [11]

2.EXCESS SODIUM INTAKE :

Excess sodium leads to hypertension by increasing fluid volume and preload, thereby increasing cardiac output. Sodium excess also affects vascular reactivity and renal function which inturn leads to increased blood pressure. [12] [13]

The Intersalt study which was conducted in 32 countries projected that a 100 mmol/day lower sodium intake over a lifetime would result in a 9mmHg smaller rise in systolic BP from 25 to 55 years of age. It demonstrated a clear relationship between the salt intake and the level of BP among communities.

Sodium sensitivity

Only about half of the patients with high sodium intake develop hypertension which suggests a variable degree of blood pressure sensitivity to sodium.

The proposed mechanisms for sodium sensitivity are defect in renal sodium excretion, increased activity of the sodium hydrogen exchanger, increased sympathetic nervous system activity, increased calcium entry into vascular smooth muscle & impaired nitric oxide synthesis. [12] [14] [15] [16] [17] Sodium sensitivity increases with advancing age and is found to be

more in women than men. [18] [19]Blacks have greater frequency of salt sensitivity.

3.ALCOHOL INTAKE :

Excessive alcohol intake is an important cause for hypertension. Excess consumption accounts for 5% to 30% of all hypertensive patients. Several studies including the Intersalt Study have shown a strong and independent positive relationship between alcohol intake and increase in blood pressure.

Alcohol intake has been found to have a biphasic effect on blood pressure. Smaller doses of alcohol has a vasodilatory effect and lowers blood pressure, but as alcohol consumption increases blood pressure increases leading to hypertension.

This dose - response characteristics varies from individual to individual depending upon various factors such as body surface area, gender and race.

The mechanism for the alcohol induced rise in blood pressure is associated with the activation of, or increased responsiveness to the sympathetic nervous system.

4.PHYSICAL ACTIVITY :

Sedentary individuals have 20 to 50% increased risk of developing hypertension. Observational and experimental studies have demonstrated the role of physical inactivity and its association with hypertension.

5.SMOKING :

Tobacco smoking has been found to cause acute rise in blood pressure. But ,whether prolonged smoking leads to sustained hypertension is not yet proved.

6.ROLE OF STRESS :

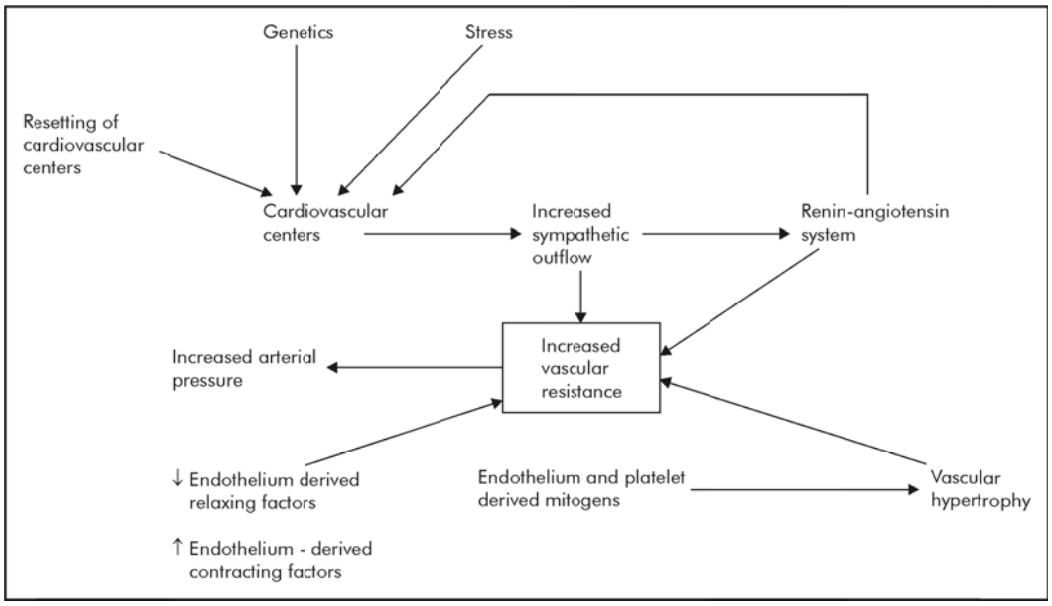


FIG 4. MECHANISM OF STRESS INDUCED HYPERTENSION

Stress directly stimulates sympathetic outflow which inturn interacts with RAAS, high sodium intake & insulin resistance leading to rise in BP.

DETERMINANTS OF BLOOD PRESSURE

There are five important factors which are responsible for maintaining the arterial blood pressure. Following are the five factors:

1.Cardiac output

2.Peripheral resistance

3.Elasticity of the arterial walls

4.Blood volume

5.Volume of the vascular space

1.CARDIAC OUTPUT :

When the ventricle contracts , more blood enters the already partially filled arteries, and the pressure on the arterial wall rises.(This is the pressure during systole). The arterial walls are stretched, the pressure rises and then falls as blood leaves the arterial system. Cardiac output influences the systolic blood pressure. Increase in cardiac output increases systolic pressure, and a decrease reduces the pressure.

2.PERIPHERAL RESISTANCE :

When resistance to flow is increased,the pressure is high and when the resistance is reduced , the pressure falls. The frictional resistance to flow of blood depends upon lumen of blood vessels, viscosity of blood and velocity of blood flow.

a.Lumen of blood vessels:

The most important factor is the lumen of vessels , especially that of arterioles which are the resistance vessels. If the lumen is narrowed (by vasoconstriction) the pressure is increased. If the lumen becomes wider (by vasodilatation) the pressure is decreased. Peripheral resistance influences the diastolic pressure more than the systolic , though both may be affected.

b.Viscosity of blood:

When the viscosity of blood is reduced (e.g. in anaemia) resistance is low; it is high when the viscosity is increased (e.g. polycythemia).

c.Velocity of blood flow:

Increased velocity of blood flow tends to increase the frictional resistance. Normally, flow in blood vessels is laminar , but becomes turbulent when there is obstruction in a vessel or the surface is roughened

(e.g. atherosclerosis). Turbulent flow sets up eddy currents and the resistance to flow is much increased.

However, the moment to moment adjustments of resistance is brought about by alterations in the lumen size by the vasomotor tone.

3. ELASTICITY OF THE ARTERIAL WALLS :

The large arteries are elastic and distensible and it is the elasticity of the arterial walls that is responsible for the origin and maintenance of the diastolic pressure.

If the arteries were rigid inelastic tubes, the pressure on the walls will rise steeply when blood enters the vessel during systole, and during diastole when no blood enters, the pressure will drop to zero.

Because the arteries are elastic , they stretch when blood enters during systole and prevent a large rise in systolic pressure. During diastole, when the entry of blood ceases, the arterial walls recoil, and this is responsible for the diastolic pressure.The recoil also acts as a secondary pump to push blood along the vessels during diastole.

The elastic recoiling of the arterial walls and the peripheral resistance in the arterioles are responsible for converting the intermittent flow of blood in the arteries to a continuous flow.

4.BLOOD VOLUME :

Increase in blood volume causes the arterial system to be overfilled and raises both systolic and diastolic blood pressures. A reduction in blood volume reduces the blood pressure.

5.VOLUME OF THE VASCULAR SPACE :

If the volume of the vascular space is increased by dilatation of the arterioles and capillaries, the blood pressure is reduced. If the vascular space is decreased , blood pressure is increased.

The blood volume and vascular space do not change much under normal circumstances. The elasticity also does not change , except very gradually with age over a long period of time or as a result of disease.

Hence, the day to day regulation of arterial blood pressure is by changes in the cardiac output and peripheral resistance.

The amount of blood entering the arteries is determined by the cardiac output. Blood leaving the arteries is determined by the peripheral resistance. Hence, if cardiac output or peripheral resistance or both are increased, blood pressure rises. If cardiac output or peripheral resistance or both are decreased blood pressure falls.

PHYSIOLOGY OF BLOOD PRESSURE

HOMEOSTASIS

The basic equation in the physiology of blood pressure is

Blood pressure = cardiac output × peripheral resistance

Cardiac output = Heart rate × stroke volume

Blood volume varies directly with total body sodium content because sodium is the predominant extracellular solute that retains water within the extracellular space.

ROLE OF KIDNEYS

The primary function of the kidneys is to regulate sodium and water excretion and consequently , they also play a dominant role in the long term control of BP.

The most important and fundamental mechanism in determining the long term control of blood pressure is the renal fluid - volume feedback system. Through this feedback system, the kidneys regulate arterial pressure by altering renal excretion of sodium and water, thereby controlling circulatory volume and cardiac output. Changes in BP, in turn directly influence the renal excretion of sodium and water, thereby

providing a significant feedback system for controlling extracellular fluid volume, cardiac output, and BP.

Two important renal mechanisms play a significant role in the long term control of blood pressure.

In the first mechanism, extracellular fluid volume is regulated by coupling the magnitude of urinary salt and water excretion and the related changes in blood volume and cardiac output , to changes in renal perfusion pressure.This phenomenon is called pressure natriuresis which is explained by Guyton and his co-workers. [20] [21]

In the second mechanism , Renin-Angiotensin-Aldosterone System (RAAS) is employed. It has a direct control over peripheral vascular resistance and reabsorption of sodium and water in renal tubules. RAAS is the long term regulator of blood pressure homeostasis . [22] [23]

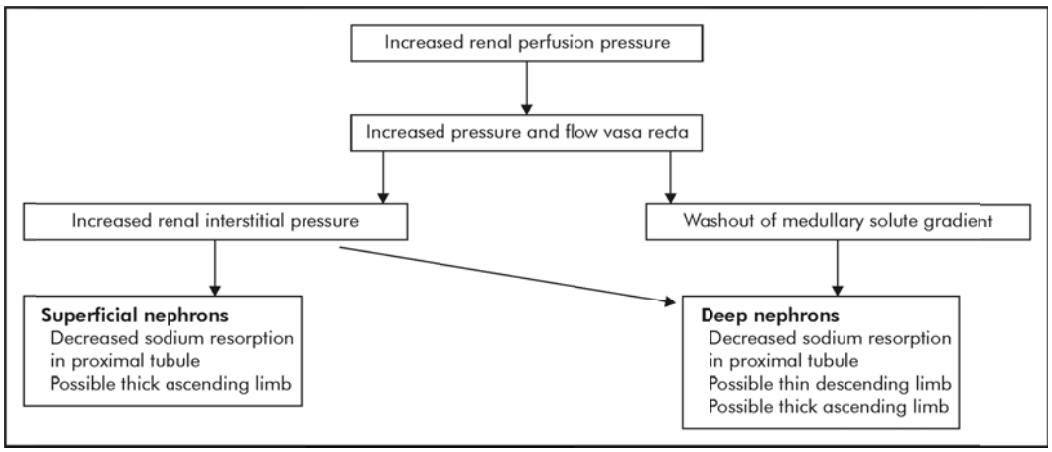
I . PRESSURE NATRIURESIS:

Pressure natriuresis is the central component of the negative feedback system which is responsible for the long term control of blood pressure. Pressure natriuresis is defined as an increase in sodium and water excretion by kidneys that occurs when arterial pressure rises.

The magnitude of urinary sodium excretion is a direct function of the renal arterial perfusion pressure.The level of perfusion pressure alters sodium excretion by changing the peritubular hydrostatic pressure.

As the perfusion pressure increases , peritubular hydrostatic pressure also increases which results in decreased sodium reabsorption and increased sodium excretion.

FIG 5. PROPOSED MECHANISMS OF PRESSURE NATRIURESIS



Various biophysical factors have been found to contribute to pressure natriuresis.These include medullary blood flow, renal interstitial hydrostatic pressure (RIHP), and renal autacoids such as angiotensin II, prostaglandins, nitric oxide and kinins.

Increased renal perfusion pressure leads to a significant increase in RIHP, kinins, prostaglandin E_2, and nitric oxide while it decreases angiotensin II.

1.RIHP:

Elevated renal perfusion pressure significantly increases RIHP, even in the absence of increased GFR and renal blood flow. [24] Pressure natriuresis can be attenuated but cannot be abolished by preventing the rise in RIHP in reponse to perfusion pressure. [25]

The exact mechanism by which RIHP affects tubular reabsorption is not known. It appears to be associated with changes in permeability of tight junctions in the proximal tubules to sodium, redistribution of apical sodium transporters and release of prostaglandin E_2.

2.NITRIC OXIDE :

Nitric oxide plays a significant role in renal hemodynamics and hence influences BP. [26] Renal medullary blood flow has an important role in maintaining blood pressure homeostasis. Nitric oxide is tonically active in the medullary circulation and regulates medullary renal vascular resistance, natriuresis and diuresis. [27]

Reduction in nitric oxide production enhances pressure natriuresis response followed by reduction in medullary blood flow, RIHP and sodium excretion without corresponding changes in total or cortical renal blood flow or GFR. [28]

3. KININS :

Kinins produce pressure natriuresis by inhibiting sodium reabsorption in the distal part of the nephron or by producing changes in the deep nephron reabsorption.

Kinins affect sodium reabsorption in three ways : i. Direct effect on the transport of sodium along the nephron, ii. A vasodilator effect, iii. Changes in the osmotic gradient of renal medulla.

4. METABOLITES OF ARACHIDONIC ACID :

Arachidonic acid is an important component of cell membrane. It is metabolised into hydroxyeicosatetraenoic acid (20-HETE) and epoxyeicosatrienoic acids (EETs) by cytochrome P450 enzymes.

Both EETs and 20-HETEs have a significant impact on renal vascular tone and sodium excretion and hence regulates pressure natriuresis.

These metabolites inhibit Na^+/K^+ - ATPase activity and promotes internalisation of NHE3 proteins at the brush border of proximal tubule thereby inhibiting proximal tubule renal transport and increasing urinary sodium excretion.

II . RENIN ANGIOTENSIN ALDOSTERONE SYSTEM :

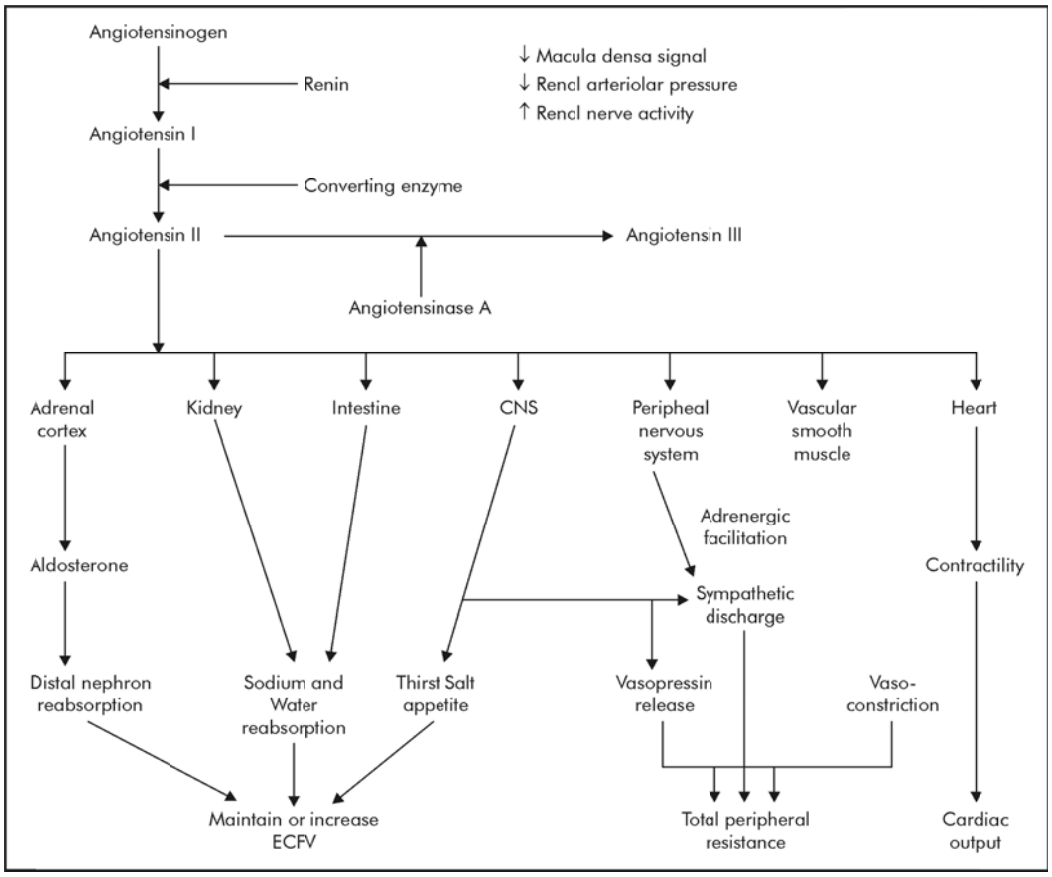


FIG 6.Schematic diagram of renin - angiotensin - aldosterone system.

Renin is a glycoprotein hormone which is secreted by juxtaglomerular cells of kidney .The signals for renin release include i.decreased signal from macula densa which detects changes in the load of sodium chloride delivered, ii.decreased renal arteriolar pressure and iii.increased renal nerve activity.

Renin is a proteolytic enzyme which acts on its substrate angiotensinogen , which is a plasma protein. Angiotensinogen is secreted from the liver and is converted to Angiotensin I with the help of renin.

During the passage of Angiotensin I through lungs , it is converted into Angiotensin II by a converting enzyme which is present on the surface endothelial cells of pulmonary vessels. Angiotensin II is rapidly inactivated by enzymes called angiotensinases.

Angiotensin II is the biologically active product of the juxtaglomerular Renin – Angiotensin system and is a vasoconstrictor and stimulates aldosterone.

ACTIONS OF ANGIOTENSIN II

1.Aldosterone cortex :

Angiotensin II stimulates the secretion of aldosterone from adrenal cortex. When there is a reduction of ECF volume or blood volume or Nacl concentration, aldosterone secretion is increased through the Renin-Angiotensin mechanism. Aldosterone promotes sodium reabsorption in the renal tubules, with chloride and water following sodium , and thus restores fluid and salt balance.

2. Cardiovascular system :

The most prominent action of Angiotensin II is vasoconstriction produced directly as well as by enhancing adrenaline or nor-adrenaline release from adrenal medulla and by increasing central sympathetic flow.

Angiotensin II also increases force of myocardial contraction by promoting calcium reflux and influences cardiac output.

3.Renal system :

In addition to exerting indirect effect on kidney through aldosterone, A- II promotes Na^+/K^+ exchange in proximal tubules which leads to sodium, chloride and bicarbonate reabsorption. Further, it reduces renal blood flow and produces intrarenal hemodynamic effects which normally results in sodium and water retention.

4.CNS :

Angiotensin II induces drinking behaviour and ADH release which leads to plasma volume expansion. It also increases central sympathetic outflow contributing to the pressor response.

5.Peripheral nervous system :

It releases adrenaline from adrenal medulla, stimulates autonomic ganglia, and increases the output of nor- adrenaline from adrenergic nerve endings.

Thus, Renin- Angiotensin-Aldosterone system plays a major role in the blood pressure homeostasis.

PATHOPHYSIOLOGY OF HYPERTENSION

ALTERED RENAL PHYSIOLOGY:

Essential hypertension is primarily due to an abnormal kidney which leads to impaired excretion of sodium. [29]Various hypotheses have been proposed to explain that , abnormal sodium retention by the kidneys is the main initiating event for hypertension.

1.GUYTON'S HYPOTHESIS :

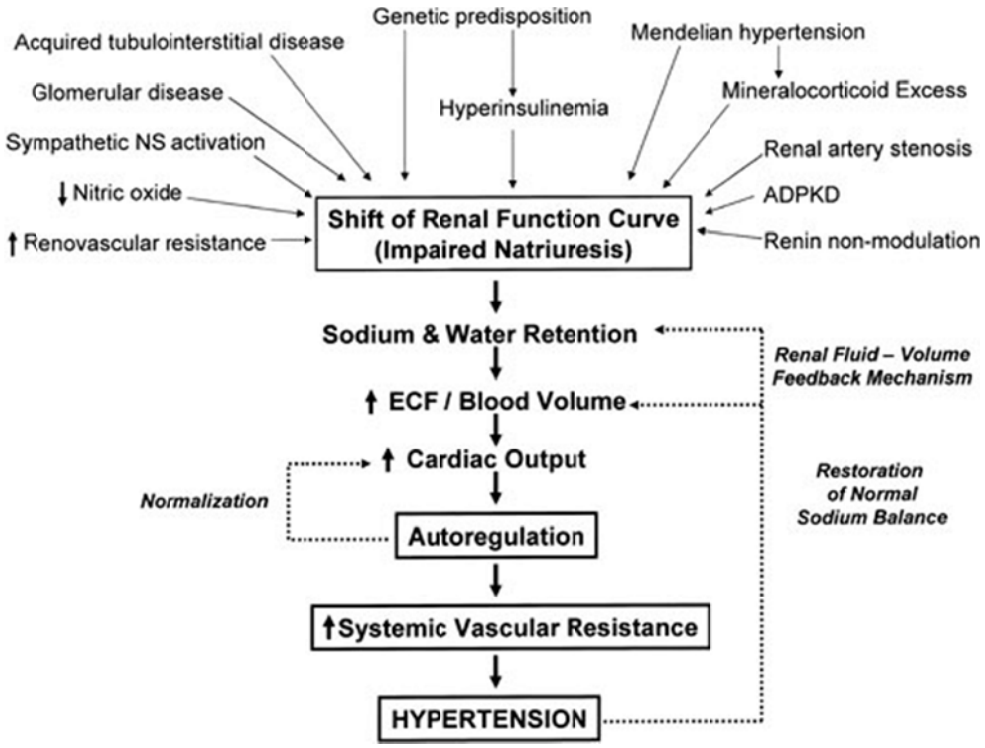
Guyton's hypothesis states that derangements in the renal fluid – volume pressure control mechanism forms the basis of virtually all hypertensive states.

In every hypertensive state , there exists an underlying abnormality in the intrinsic natriuretic capacity of the kidney so that the daily salt intake cannot be excreted at a normal BP, and the development of hypertension is necessary to induce a pressure natriuresis that allows the kidney to excrete the daily salt intake. Normal sodium balance and ECF volume are maintained but at the expense of systemic hypertension.

Depending upon the etiology of hypertension, the underlying cause for the abnormality in the natriuretic capacity of the kidney varies. In

essential hypertension , some underlying abnormality increases renal avidity for sodium. For example, in patients with metabolic syndrome, hyperinsulinemia increases proximal tubular sodium reabsorption. Increased Angiotensin II levels and sympathetic nervous system activity also enhances sodium reabsorption. Mineralocorticoids enhance distal tubular sodium reabsorption. Renal parenchymal disease causes nephron loss, resulting in a natriuretic in a natriuretic defect. Impaired natriuresis also occurs due to defect in renal endothelin or nitric oxide levels.

FIG 7. GUYTON 'S HYPOTHESIS – ABNORMAL RENAL SODIUM HANDLING LEADING TO HYPERTENSION .



To date , each of the genetic causes of hypertension that have been elucidated has been found to be related to an abnormality of renal sodium handling. For example, Liddle's syndrome occurs due to an abnormality in sodium channels in the distal nephron which leads to enhanced distal tubular sodium reabsorption.

Guyton's hypothesis states that this impaired natriuretic capacity of the kidney leads to sodium and water retention initially which in turn leads to ECF volume expansion and increased cardiac output with hypertension. But, this phase of volume expansion and high cardiac output is short lived.

In this high cardiac output state, autoregulatory vasoconstriction of each vascular bed matches the blood flow to the metabolic requirements of the tissues.This phenomenon of circulatory autoregulation results in an increase in the systemic vascular resistance (SVR). Therefore, hypertension that was initially caused by high cardiac output becomes high SVR hypertension.

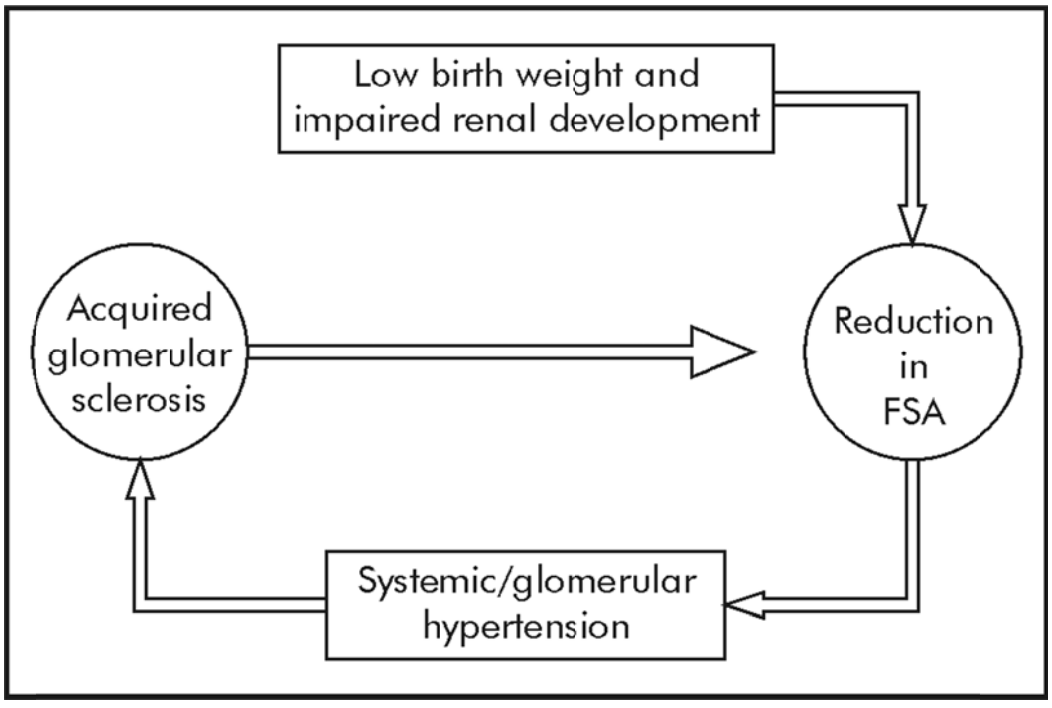
The development of hypertension represents a protective mechanism, because it induces the kidney to undergo a pressure natriuresis and diuresis , thereby restoring normal salt balance and returning ECF volume to normal.

2. BRENNER'S HYPOTHESIS :

Brenner et al[30] in 1988 stated that the nephron endowment at birth is inversely related to the risk of developing hypertension later in life.

The congenital reduction in the number of nephrons or in the filtration surface area (FSA) per glomerulus , limits the ability to excrete sodium, raises the blood pressure, and sets off an vicious circle, whereby systemic hypertension begets glomerular hypertension which begets more systemic hypertension. [31]

FIG 8. SCHEMATIC DIAGRAM OF BRENNER'S HYPOTHESIS

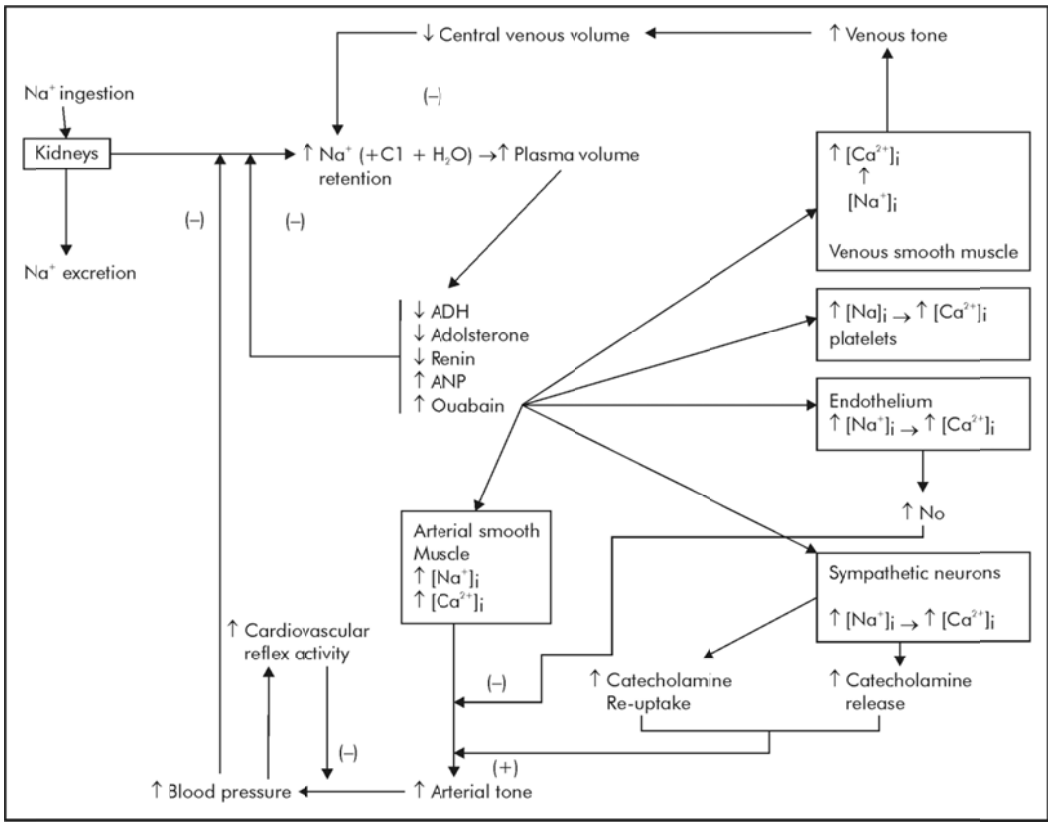


Impaired renal development or reduction in FSA leads to systemic HT which in turn leads to glomerular HT and the vicious cycle continues.

3. BLAUSTEIN'S HYPOTHESIS :

According to Blaustein [32], when plasma volume is expanded, Ouabain, an endogenous digitalis like inhibitor of sodium pump is secreted. It increases intracellular sodium and mobilises calcium from intracellular stores. Ultimately arterial tone is increased which leads to the development of essential hypertension. In this hypothesis also, sodium retention is the basic mechanism.

FIG 9. BLAUSTEIN'S HYPOTHESIS – MECHANISM OF RENAL SODIUM RETENTION.



4. RENIN –ANGIOTENSIN – ALDOSTERONE SYSTEM :

Renin plays a significant role in the pathogenesis of hypertension. [33] In essential hypertension, normally, low levels of renin are expected. But , majority of the patients with essential hypertension show inappropriately normal or even elevated plasma renin levels. About 20% are found to have high renin levels, and about 30% have low renin values, with the remaining half distributed between these two extremes.

Three mechanisms have been offered for such variations in renin levels. The mechanisms are described below :

A. Nephron heterogeneity in essential hypertension : [34]

Nephron heterogeneity with unsuppressible renin secretion is proposed as the cause for essential hypertension.

Within the kidneys, there exists a functional and structural basis for the abnormal renin secretion and impaired sodium excretion that are characteristics of hypertensive states.

Hypothesis - there is nephron heterogeneity in essential hypertension :

i. There are ischemic nephrons with impaired sodium excretion intermingled with adapting hyperfiltering hypernatriuretic nephrons.

ii. Renin secretion is high from ischemic nephrons and low from hyperfiltering nephrons.

iii. The inappropriate circulating renin-angiotensin level impairs sodium excretion because:

a. In the adapting hypernatriuretic nephrons

- It increases tubular sodium reabsorption.

- It enhances tubuloglomerular feedback mediated afferent constriction.

b. As the circulating renin level is diluted by non- participation of adapting nephrons, it becomes inadequate to support efferent tone in hypoperfused nephrons.

iv. A loss of nephron number with age and from ischemia further impairs sodium excretion.

B. Theory of non – modulation

About half of the hypertensive patients have normal and high renin levels. Williams and Hollenberg proposed a theory of non–modulation [35] which states that defective feed – back regulation of the renin – angiotensin system within the kidneys and the adrenal glands is responsible for this normal and high renin levels.

In normal individuals , the responsiveness of the target tissues to angiotensin II is modulated with their level of dietary sodium intake. Sodium restriction enhances adrenal secretion of aldosterone and reduces vascular response, leading to sodium loading which inturn suppresses adrenal response and enhances vascular response , particularly within the renal circulation.

Sodium restriction reduces renal blood flow facilitating sodium conservation while sodium loading increases renal blood flow promoting sodium excretion. All these effects are mediated by angiotensin II levels which increases with sodium restriction and decreases with sodium loading.

Non – modulation is characterized by abnormal renal and adrenal responses to Angiotensin II and dietary salt loads. [36] This is due to an abnormally regulated and fixed level of angiotensin II , which does not increase adrenal secretion of aldosterone in response to sodium restriction and in the renal circulation , does not increase renal blood flow in response to sodium loading.

This hypothesis is supported by the fact that suppression of angiotensin II by ACE inhibitors in such non – modulators , corrects both the adrenal and renal defects.

c. Low renin essential hypertension

Low renin levels are found in about 40% of patients with essential hypertension . Volume expansion with or without mineralocorticoid excess has been proposed as the possible mechanism for low renin hypertension.

Fishar et al focussed on adrenal and pressure responsiveness to angiotensin II which depends on the dietary salt intake in patients with normal renin hypertension , low renin hypertension and normal controls.

Comparison of patients with normal renin hypertension and non-modulating essential hypertension with normal plasma renin activity showed some similarities which include

i. Salt sensitivity of the blood pressure

ii. Blunted plasma aldosterone responses to angiotensin II and upright posture after dietary sodium restriction for 5 days.

iii. Relatively low basal plasma aldosterone levels.

When normal controls and modulating hypertensive subjects are compared , there were significant differences between them which disappeared when dietary salt intake was increased.

With high sodium intake , plasma angiotensin II activity is suppressed which leads to resensitisation of angiotensin II receptors and improved responsiveness of target tissues to angiotensin II.

With sodium restriction , there is blunted responsiveness to angiotensin II owing to continuing generation of angiotensin II and angiotensin receptor downregulation in target tissues.

An impaired hydroxy steroid dehydrogenase type 2 (HSD II B2) activity plays a significant role in the pathogenesis of essential hypertension in some patients.

Apparent mineralocorticoid excess (AME) is a rare monogenic juvenile hypertensive syndrome which occurs due to mutations in the HSD II B2 gene. In AME , altered HSD enzyme activity causes excessive stimulation of the mineralocorticoid receptor by cortisol which leads to hypokalemia, sodium retention and salt dependent hypertension. [37] [38]

The prevalence of mutations in HSD II B2 in general population of patients with essential hypertension presently unknown. It is important to seek the diagnosis of AME by genetic and clinical studies because specific therapy such as spironolactone is available for this disease which causes ready remission .

TWO FORMS OF VASOCONSTRICTION IN PRIMARY HYPERTENSION

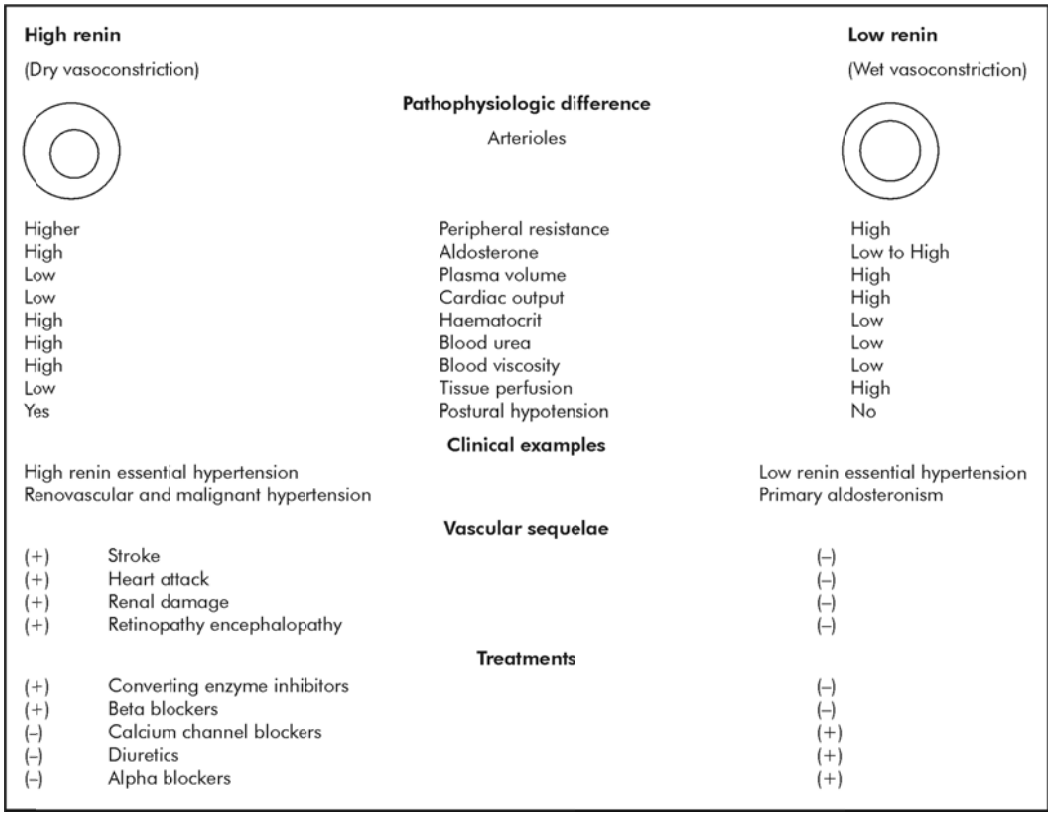
Two forms of vasoconstriction , one mediated by sodium – volume forces and the other mediated by renin – angiotensin system are essential to maintain normal BP homeostasis. When these mechanisms are impaired , hypertension occurs. These spectral patterns of vasoconstriction seen in seen in extreme forms of hypertension also operate in primary hypertension.

Laragh and his co-workers attached a great significance to various plasma renin activity levels (PRA) levels found in patients with essential hypertension. According to their view , based on the renin levels , the relative contribution of vasoconstriction and body fluid expansion to the pathogenesis of hypertension can be identified.

According to the " bipolar vasoconstriction – volume analysis", arteriolar vasoconstriction by angiotensin II is predominantly responsible for the hypertension in patients with high renin whereas volume expansion is predominantly responsible in those with low renin. Both lead to increased peripheral resistance which is the common characteristic of all hypertension.

Apart from the similarity in peripheral resistance,the two forms of vasoconstriction are totally different in their pathophysiology , complications and treatment [39] as shown in the figure 10.

FIG 1O. HIGH BP MECHANISMS BASED ON RENIN LEVELS



High renin (Dry vasoconstriction)	Pathophysiologic difference	Low renin (Wet vasoconstriction)
	Arterioles	
Higher	Peripheral resistance	High
High	Aldosterone	Low to High
Low	Plasma volume	High
Low	Cardiac output	High
High	Haematocrit	Low
High	Blood urea	Low
High	Blood viscosity	Low
Low	Tissue perfusion	High
Yes	Postural hypotension	No
	Clinical examples	
High renin essential hypertension Renovascular and malignant hypertension		Low renin essential hypertension Primary aldosteronism
	Vascular sequelae	
(+) Stroke		(–)
(+) Heart attack		(–)
(+) Renal damage		(–)
(+) Retinopathy encephalopathy		(–)
	Treatments	
(+) Converting enzyme inhibitors		(–)
(+) Beta blockers		(–)
(–) Calcium channel blockers		(+)
(–) Diuretics		(+)
(–) Alpha blockers		(+)

The predominance of activity of either pole depresses the activity at other pole whereas both vasoconstrictive forces may assert their influence when renin levels are in the medium range.

The spectrum of hypertensive disorders are stratified according to their renin – sodium relationship as shown in FIG 11.

FIG 11. SPECTRUM OF HYPERTENSIVE DISORDERS

The Laragh vasoconstriction – volume spectrum of clinical hypertension

PRA				Body Na^+
High	VASOCONSTRICTION ↑	Malignant hypertension Unilateral renovascular High renin essential hypertension Pheochromocytoma	VOLUME ↓	Low
Medium		Medium-renin essential hypertension Bilateral renovascular hypertension		Normal
Low		Low-renin essential hypertension Primary hyperaldosteronism		High

Normal BP = (PRA) X (Na^+ → Volume)

BP = Blood pressure ; PRA = Plasma renin activity .

Normal subjects maintain and defend normal blood pressure by curtailing renal renin secretion in reaction to a rise in sodium intake or autonomic vasoconstriction or by proportionally increasing renin secretion in reaction to either sodium depletion or hypotension from fluid or blood loss or a neurogenic fall in blood pressure.

Hypertensive subjects sustain their higher blood pressures by renal secretion of too much renin for their Na^+ volume states or by renal retention of too much Na^+ volume for their renin level , which often fails to fully turn off as it does in normal subjects.

High renin hypertensive subjects are proportionately more vasoconstricted with poor tissue perfusion and therefore most susceptible to cardiovascular tissue ischemic damage.

5. SHEPHERD'S HYPOTHESIS :

In normal individuals , when there is an increase in the blood pressure or central venous pressure , the baroreceptors are activated and they reduce heart rate and lower blood pressure, respectively, by vagal stimulation and sympathetic inhibition.

When there is sustained hypertension, resetting of the baroreceptor reflexes occur due to structural and functional changes so that an increase in blood pressure evokes less reduction in heart rate. [40]

Shepherd's hypothesis states that the decreased inhibition of the vasomotor center which results from resetting of the arterial baroreceptors may be responsible for increased sympathetic outflow and thereby in the perpetuation of hypertension. [41]

6. SALT DEPENDENT HYPERTENSION :

It has been proposed that hypertension has two phases. An early phase in which the elevations in blood pressure are mainly episodic and are mediated by a hyperactive sympathetic nervous system or renin-angiotensin system. The second phase is characterised by persistently elevated BP which is primarily mediated by an impaired ability of the kidney to excrete sodium chloride salt.

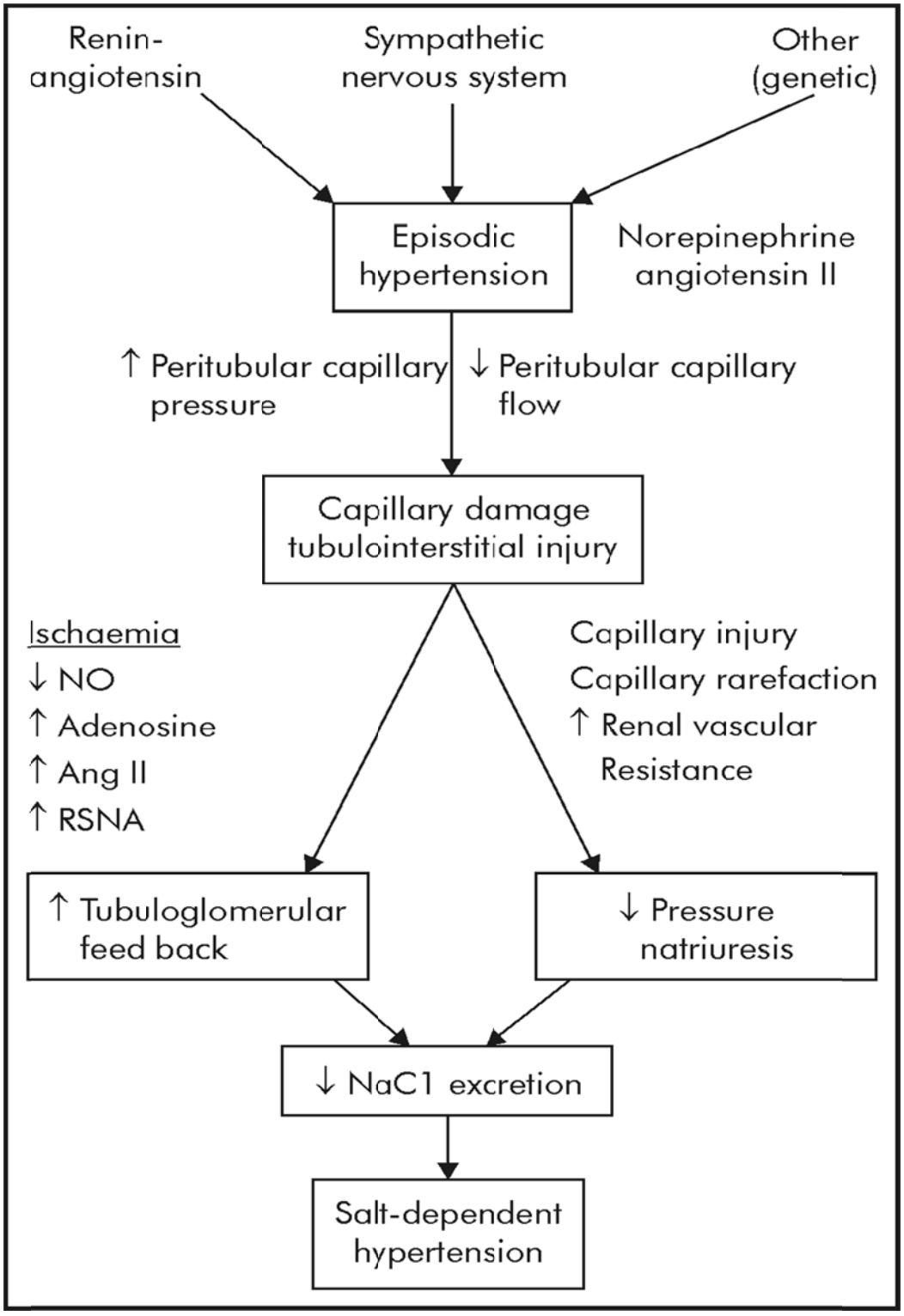


FIG 12. PATHOGENESIS OF SALT DEPENDENT HYPERTENSION

The acute norepinehrine or angiotensin II mediated elevation in blood pressure is transmitted to the peritubular capillaries of the kidney in association with a reduction in blood flow, secondary to the vasoconstrictive properties of these substances. Capillary damage and tubulointerstitial injury with fibrosis results.

The local ischemia stimulates (adenosine , ang II , renal sympathetic nerve activity) or inhibits (nitric oxide , prostaglandins , dopamine) vasoactive mediators , resulting in NaCl reabsorption due to enhanced tubuloglomerular feedback.The capillary damage and increase in renal vascular resistance also blunts pressure natriuresis mechanism.

The consequences of both enhanced tubuloglomerular feedback and impaired pressure natriuresis is an acquired functional defect in sodium chloride excretion . This results in the resetting of the pressure – natriuresis curve to a higher pressure in order to restore sodium balance back to normal. [42]

This is proposed as the major mechanism for the development of salt dependent hypertension. Thus , essential hypertension may be a type of acquired tubulointerstitial renal disease.

In conclusion , this hypothesis links early, episodic, salt independent hypertension with the later development of a persistent salt dependent hypertension with a new concept that it is mediated by acquired tubulointerstitial and peritubular capillary injury.

The strength of this hypothesis is that it unites many prior hypotheses into one pathway ; including that of **Guyton et al** on impaired pressure natriuresis [20], of **Brenner** on reduced nephron number [39], of **Sealey and Laragh** on activation of the renin angiotensin II system [34], of Cowley et al on the role of medullary ischemia [26], of **Kurokawa** on enhanced tubuloglomerular feedback [43], of **Julius** on the role of the sympathetic nervous system in early hypertension [44].

In addition , this hypothesis potentially provides answers to many questions not easily addressed by other individual hypothesis.

REVIEW OF LITERATURE

Many epidemiological studies have shown a strong relationship between dietary salt intake and hypertension. Few studies regarding the association of salt intake and blood pressure are mentioned here.

1.**Carherine E Huggins et al** assessed 24 hour urinary sodium and potassium excretion and examined the relationship to blood pressure within a population of middle aged and older Australian adults. In the five hundred and eighty seven participants with blood pressure measurements , urinary sodium and the sodium to potassium ratio were both associated with systolic blood pressure even after adjustment for age, sex and BMI.The study demonstrated that sodium intake is positively associated with blood pressure. (45)

2**. Rosa M.Ortega et al** studied about the sodium intake of a representative sample in the Spanish young and middle aged population. Sodium intake was measured by 24 hour urinary sodium excretion. In this study, urinary sodium excretion significantly correlated with systolic and diastolic blood pressure .About 88% of the subjects in the study group had salt intakes above 5g/day. Male subjects and participants with higher BMI were found to be associated with high urinary sodium excretion . (46)

3.B.M.Y CHEUNG et al studied seventy Chinese patients with untreated hypertension and forty seven normotensive controls. For each subject , blood pressure and 24 hour urinary sodium & potassium excretion were measured. 22 hypertensive patients underwent ambulatory blood pressure monitoring. In hypertensive patients, the diastolic BP directly correlated with 24 hour urinary Na excretion while in normotensive controls , it did not correlate with 24 hour urinary sodium excretion. Even patients who underwent ambulatory blood pressure monitoring showed a significant correlation between diastolic BP and sodium excretion. Systolic blood pressure did not correlate with sodium excretion , although it increased with advancing age of the patient. (47)

4.RA JAN et al studied the relationship of 24 hour urinary Na^+ and K^+ excretion, Na^+/K^+ molar ratio and body mass index with blood pressure in hypertensive patients and normotensive controls in Kashmir. 24 hour urinary Na^+ excretion, Na^+/K^+ molar ratio and body mass index were significantly increased in hypertensive people when compared to normal individuals. But , 24 hour urinary K^+ excretion was low in hypertensive patients. Thus , Na^+ and K^+ excretion , Na^+/K^+ molar ratio and BMI were found to have a direct role in the etiology or perpetuation of hypertension in Kashmir, which was attributed to high intake of salt tea in this population. (4)

5.KUO – LIONG CHIEN et al reported about the role of 24 hour urinary sodium excretion in the development of hypertension among ethnic Chinese community. In this prospective cohort study from Chinese community, a significant J-shaped relationship was observed between 24 hour urinary sodium excretion and the risk of hypertension. Subjects in the highest quartile of urinary Na^+ excretion and higher baseline BP had twofold increased risk of hypertension when compared to those in the lowest quartile of urinary Na^+ excretion and lower blood pressure. High urinary Na^+ excretion was associated with significant risk of hypertension in ethnic Chinese population. (48)

6.INTERSALT (3) , an international epidemiological study examined the relation between dietary sodium intake (based on 24 hour urinary sodium excretion) and BP in more than ten thousand individuals, aged between twenty and fifty nine years, from fifty two countries around the world. Sodium excretion correlated strongly and positively with blood pressure while potassium excretion correlated negatively with blood pressure in individual subjects, even after controlling for confounding variables. Na^+/K^+ molar ratio also correlated positively with blood pressure. Age, BMI and high alcohol intake had strong influence on blood pressure in individual subjects . Among 52 countries in the study, four countries recorded lower blood pressure owing to low salt intake in these regions.

7.SONJA L. CONNOR et al studied the relationship of blood pressure with age , body weight and multiple dietary factors among the members of more than two hundred randomly selected families. Age , bodyweight and heart rate were independently and positively correlated with blood pressure. A strong familial component was identified for urinary Na^+ and K^+ excretion and for systolic BP. In females, urinary sodium and potassium excretions correlated positively with diastolic BP. But , this relationship did not persist after controlling for confounding variables such as age and body weight. In males, intake of dietary factors such as potassium, calcium and phosphorous correlated positively with systolic BP even after controlling for confounding variables.This is in contrast to other studies which showed a negative correlation between potassium intake and blood pressure. (49)

8.SUSAN HEDAYATTI et al studied the correlation between urinary sodium & potassium molar ratio and blood pressure in more than 3000 participants. 56% of the participants were women and 52% were African Americans. Urinary Na^+/K^+ molar ratio correlated positively with both systolic and diastolic blood pressure even after adjusting for serum cholesterol, smoking, diabetes mellitus, BMI and GFR . Both systolic and diastolic BP were significantly elevated in African Americans when compared to non – African Americans. (50)

AIMS AND OBJECTIVES

1.To study the association between 24 hours urinary sodium & potassium excretion and blood pressure in patients with essential hypertension.

2.Our study was based on GUYTON's hypothesis which states that individuals with impaired capacity to excrete sodium require greater increase in arterial pressure to maintain sodium balance.

3.The anticipated outcome in our study was that individuals with high urinary sodium excretion and low urinary potassium excretion were more likely to develop hypertension.

MATERIALS AND METHODS

SOURCE OF DATA :

The study was conducted in Government RajajiHospital,Madurai among patients attending outpatient clinic in general medicine.40 patients as per criteria of JNC VI report and equal number of age and sex matched controls were taken up for study.

DESIGN OF STUDY:

Our study was a randomised prospective study comparing two groups – Hypertensives and Normotensives.

PERIOD OF STUDY:

The study was conducted for a period of eight months from April 2012-November 2012.

ETHICAL APPROVAL:

Obtained from institutional ethical committee headed by DEAN,Government Rajaji hospital ,Madurai.

CONSENT :An informed written consent was obtained from all the subjects included in the study.

STUDY GROUP:

INCLUSION CRITERIA:

1.Age between 18 and 75 years.

2.Hypertension as per JNC VI report-BP – 140/90 mmHg least at three different occasions after refraining from anti-hypertensives and diuretics for atleast three weeks before the study.

3.Refraining from eating,smoking or indulging in any stressful activity 30 minutes before recordings.

EXCLUSION CRITERIA:

1.Patients with secondary hypertension.

2.Patients on NSAIDs, anti-hypertensives,diuretics.

3.Patients with congestive cardiac failure.

4.Patients with malignant hypertension.

5.Females on oral contraceptive medications.

CONTROL GROUP:

1.Same age and sex.

2.BP lower than 140/90 mmHg.

METHODOLOGY:

A detailed medical history was obtained from all the subjects. Family history of hypertension,Diabetesmellitus,cardiovascular disease and renal disease were sought. Duration of hypertension ,levels of elevated blood pressure,results and side effects of anti-hypertensive therapy were recorded. History of all the prescribed and over the counter medications,smoking,alcoholuse,weight gain and symptoms suggestive of secondary hypertension were obtained.

A complete physical examination was conducted for all the subjects which included pulse and BPmeasurements,examination of extremities for edema,examination of neck for distended veins,thyromegaly,examination of cardiovascular,respiratory,abdominal and central nervous systems,optic fundoscopic examination for any hypertensive changes. Height and weight were measured and Body mass Index was calculated as weight in kg/height in m^2.

Blood pressure was measured on three different occasions with same standard mercury sphygmomanometer in both supine and standing positions. The average of three readings was used in data analysis.

The following investigations were done in all the subjects:

1.Completehemogram

2.Urine analysis

3.Serum – sugar,urea,creatinine,calcium,phosphorus,uric acid and cholesterol

4.Serum – sodium and potassium

5.24 hours urinary sodium and potassium excretion.Na^+/K^+ molar ratio was calculated.

6.USG abdomen and pelvis

7.ChestXray

8.Electrocardiogram and Echocardiography

9.Thyroid profile

24 hour urine collection was done in our study group to measure urinary sodium and potassium excretion. All the participants were instructed to collect urine for 24 hours and not to alter their dietary pattern during collection so that the urinary sodium and potassium excretion amount was a direct measure of sodium and potassium intake of the individuals.

STASTICAL ANALYSIS:

Statistical analysis was performed using statistical software Medcalc version 12.3 for Windows. P value <0.05 was considered significant. Baseline characteristics between cases and controls were compared using student t test for quantitative variables and chi square test for qualitative variables. Relationship between different variables were analysed by partial correlation after controlling for potential confounders (age,sex&BMI). The different trends in sodium and potassium excretion depending upon age group, BMI and severity of hypertension were analysed using ANOVA.

RESULTS AND OBSERVATIONS

TABLE 1

Distribution of age among study group

GROUP	NO	AGE		P VALUE
		MEAN	S.D	
CASES	40	49.73	10.698	0.3328
CONTROLS	40	47.43	10.406	

In our study,the age of normotensive group ranged from 20-65 years whereas in the hypertensive group it ranged from 25-68 years.

The mean age in the normotensive group was 47.43 with standard deviation of 10.406.

The mean age in the hypertensive group was 49.73 with standard deviation of 10.698.

P value was 0.3328 which was not significant.

So, there was no significant difference in the distribution of age among hypertensives and normotensives.

TABLE 2

Distribution of study population in relation to gender

SEX	HYPERTENSIVES		NORMOTENSIVES	
	NO	PERCENTAGE	NO	PERCENTAGE
MALES	22	55	20	50
FEMALES	18	45	20	50
TOTAL	40	100	40	100

In our study population, 42 were males and 38 were females.52.5% were males and 47.5% were females.

In hypertensive group, there were 22 males and 18 females.55% were males and 45% were females.

In the normotensive group, there were 20 males and 20 females. 50% were males and 50% were females.

P value was 0.8228 which was not significant.This suggests that there was no significant difference in the distribution of gender among study population.

In the study population 52.38% of males were hypertensives while in females 47.37% were hypertensives.

GRAPH 1

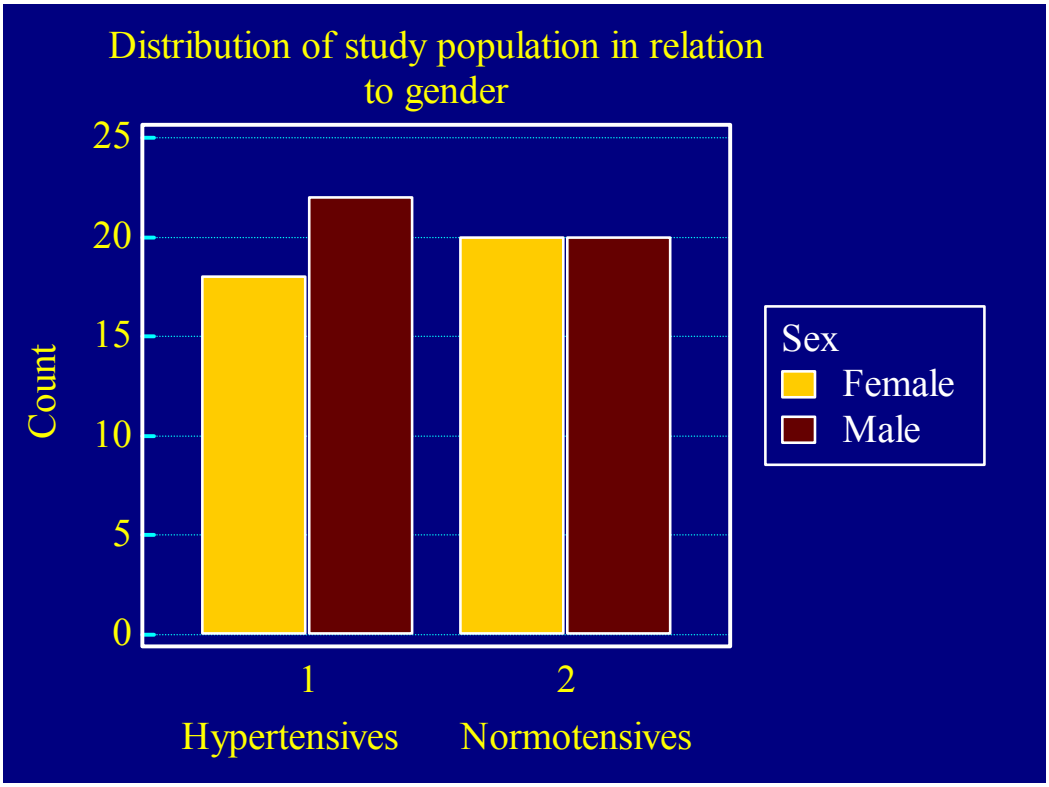

Distribution of study population in relation to gender
Count
25
20
15
10
5
0
1
2
Hypertensives
Normotensives
Sex
Female
Male

TABLE 3

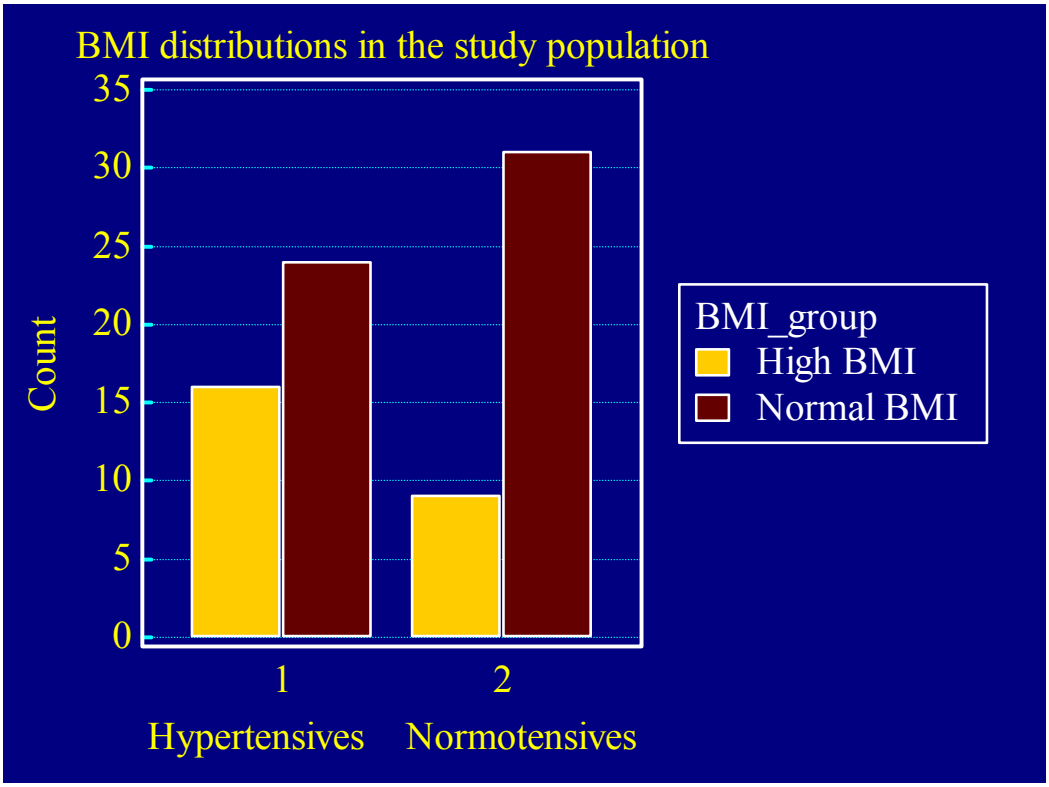
BMI distributions in the study population

BMI	HYPERTENSIVES		NORMOTENSIVES		P value
	No	Percentage	No	Percentage	
< 25	24	60%	31	77.5%	
≥ 25	16	40%	9	22.5%	
Total	40	100	40	100	0.096
MEAN	24.3020		23.479		
S.D	2.445		1.894		

The average BMI in the hypertensive group is 24.3020 ± 2.445 whereas the average BMI in the normotensive group is23.479 ± 1.8937.There was no significant difference in the BMI distributions among cases and controls as the P value is 0.096 which is not significant.

In our study population, 25 people had high BMI and 55 had normal BMI.31.2% had high BMI while 68.7% had normal BMI.Of the 40 people in the hypertensive group,16 had high BMI and 24 had normal BMI whereas in the normotensive group 9 had high BMI and 31 had normal BMI.

GRAPH 2


BMI distributions in the study population
Count
35
30
25
20
15
10
5
0
1
2
Hypertensives
Normotensives
BMI_group
High BMI
Normal BMI

40% of hypertensives had high BMI while in normotensives 22.5% had high BMI.

64% of people with high BMI were hypertensives while 43.64% of people with normal BMI were hypertensives.

TABLE 4

Comparison of serum cholesterol between hypertensives and normotensives

	Hypertensives		Normotensives		P value	Remarks
	Mean	S.D	Mean	S.D		
Serum cholesterol	193	14.768	183.15	13.275	0.0024	significant

The average cholesterol in the hypertensive group was 193 ± 14.768 whereas the average cholesterol in the normotensive group was 183.15 ± 13.275.

P value was 0.0024 which was statistically significant.This suggests that there was significant difference in the cholesterol levels among cases and controls.

TABLE 5

Comparison of serum electrolytes between hypertensives and normotensives

	Hypertensives		Normotensives		p value	Remarks
	Mean	S.D	Mean	S.D		
Serum Na	140.43	4.031	138.28	2.837	0.007	Significant
Serum K	3.90	0.387	3.79	0.287	0.127	Not significant

The average serum sodium in the hypertensive group was 140.43 ± 4.031 whereas the average serum sodium in the normotensive group was 138.28 ± 2.837.P value was 0.007 which was statistically significant.

The average serum potassium in the hypertensive group was 3.90 ± 0.387 while in the normotensive group it was 3.79 ± 0.287.P value was 0.126 which was not significant statistically.

There was significant difference in serum sodium levels among hypertensives and normotensives. Serum sodium levels were higher in hypertensives when compared to normotensives.There was no significant difference in potassium levels between the two groups.

TABLE 6

Comparison of serum calcium and phosphorus betweenhypertensives and normotensives

	Hypertensives		Normotensives		P value	Remarks
	Mean	S.D	Mean	S.D		
Serum calcium	9.590	0.534	9.440	0.605	0.2433	Not significant
Serum phosphorus	3.755	0.295	3.680	0.272	0.2409	Not significant

The mean serum calcium in the hypertensive group was 9.590 with a standard deviation of 0.534 while the mean serum calcium in the normotensive group was 9.440 with a standard deviation of 0.605 .P value was 0.2433 which was not significant.

The mean serum phosphorus in the hypertensive group was 3.755 with a standard deviation of 0.295 while the mean serum phosphorus in the normotensive group was 3.680 with a standard deviation of 0.272. P value was 0.2409 which was not significant.There was no significant difference in serum Ca^{2+} and phosphorus levels among hypertensives and normotensives.

TABLE 7

Comparison of glycemic levels between hypertensives and normotensives

	Group	No	Mean	S.D	P value	Remarks
Blood Sugar	Cases	40	103.90	9.9403	0.4371	Not significant
	Controls	40	102.45	6.2468		

The mean blood sugar was 103.90 ± 9.9403 among cases and 102.45 ± 6.2468 in controls.P value was 0.4371 which indicates there was no significant difference in the glycemic status of both the groups.

TABLE 8

Comparison of serum uric acid between hypertensives and normotensives

	Group	No	Mean	S.D	P value	Remarks
Serum Uric acid	Cases	40	5.958	0.5514	0.2001	Not significant
	Controls	40	5.775	0.7027		

The mean serum uric acid was 5.958 ± 0.5514 in the hypertensive group and 5.775 ± 0.7027 in the normotensive group.P value was 0.2001 which was not significant.

TABLE 9

Distribution of study population in relation to renal parameters

	Group	No	Mean	S.D	P value	Remarks
Serum Urea	Cases	40	36.20	6.603	0.2769	Not significant
	Controls	40	34.48	7.463		
Serum Creatinine	Cases	40	0.98	0.281	0.2920	Not significant
	Controls	40	0.92	0.267		

The mean serum urea in the hypertensive group was 36.20 with a standard deviation of 6.603while the mean serum urea in the normotensive group was 34.48 with a standard deviation of 7.463.P value was 0.2769 which was not significant.

The mean serum creatinine in the hypertensive group was 0.98 with a standard deviation of 0.281 while the mean serum creatinine in the normotensive group was 0.92 with a standard deviation of 0.267 . P value was 0.2920 which was not significant.

There was no significant difference in the serum urea and creatinine levels between the hypertensive group and normotensive group.

TABLE 10

Distribution of Blood pressure among cases and controls

Blood pressure	Group	No	Mean	S.D	P value	Remarks
Systolic BP	Cases	40	166.55	10.564	<0.0001	Highly significant
	Controls	40	115.75	5.995		
Diastolic BP	Cases	40	98.20	4.525	<0.0001	Highly significant
	Controls	40	77.70	4.784		

The mean systolic blood pressure among cases was 166.55 with a standard deviation of 10.564 while the mean systolic blood pressure among controls was 115.75 with a standard deviation of 5.995. P value was < 0.0001 which was highly significant.

The mean diastolic blood pressure was 98.20 among cases with a standard deviation of 4.525 while the mean diastolic blood pressure was 77.70 in the control group with a standard deviation of 4.784. P value was <0.0001 which was highly significant.

Both the systolic and diastolic blood pressures were significantly high among cases when compared to controls.

TABLE 11

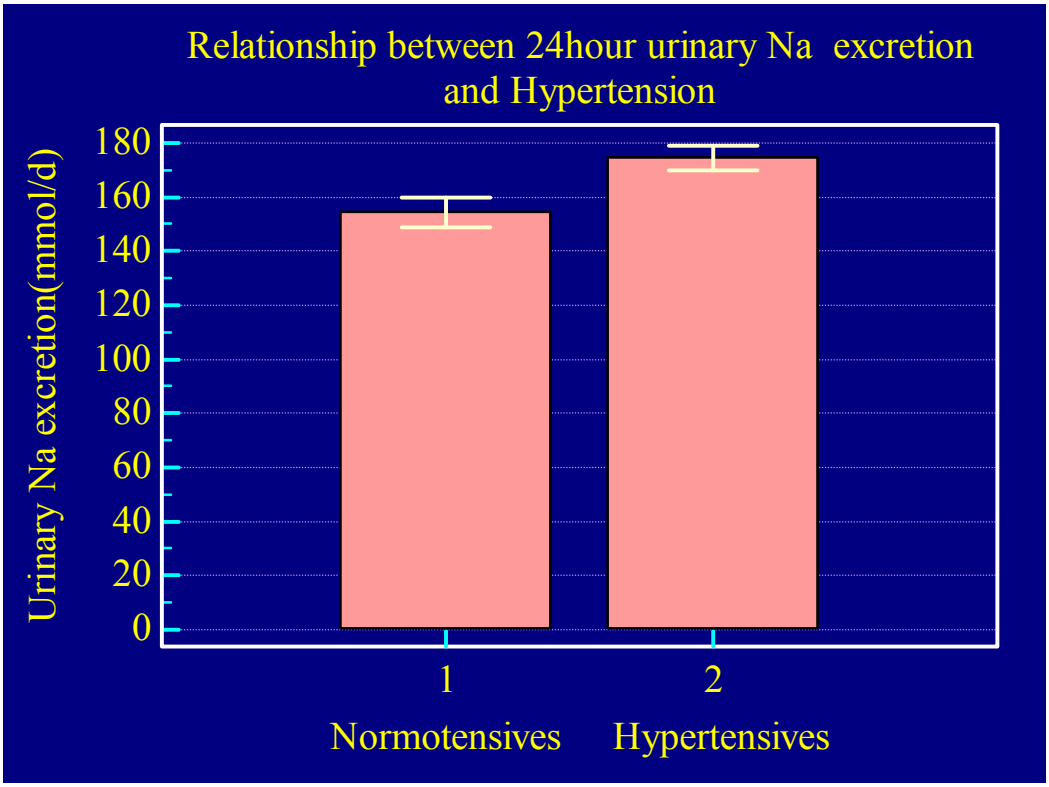
Distribution of 24 hours urinary sodium and potassium excretion among hypertensives and normotensives

Electrolytes	Group	Mean	S.D	P value
Urinary Na^+ excretion	Cases	174.550	14.551	<0.0001
	Controls	154.425	17.279	
Urinary K^+ excretion	Cases	52.850	7.343	0.2242
	Controls	54.925	7.797	
Na^+K^+ molar ratio	Cases	3.36:1		<0.0001
	Controls	2.87:1		

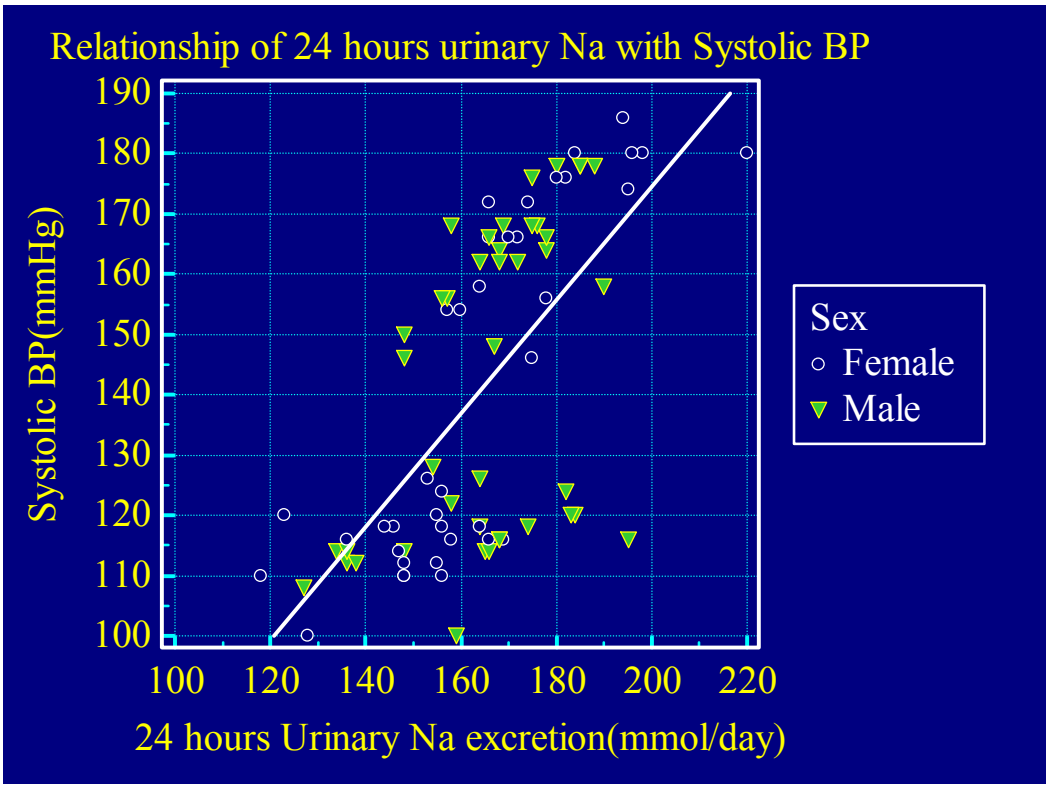
The mean 24 hour urinary sodium excretion in the hypertensive group was 174.550 ± 14.551 while the mean 24 hour urinary sodium excretion in the normotensive group was 154.425 ± 17.279. P value was <0.0001 which was highly significant.

The mean 24 hour urinary potassium excretion in the hypertensive group was 52.85 ± 7.343 while the mean 24 hour urinary potassium excretion in the normotensive group was 54.93 ± 7.797.P value was 0.2242 which was not significant.

GRAPH 3


Relationship between 24hour urinary Na excretion and Hypertension
Urinary Na excretion(mmol/d)
180
160
140
120
100
80
60
40
20
0
1
2
Normotensives
Hypertensives

GRAPH 4


Relationship of 24 hours urinary Na with Systolic BP
Systolic BP(mmHg)
190
180
170
160
150
140
130
120
110
100
100
120
140
160
180
200
220
24 hours Urinary Na excretion(mmol/day)
Sex
Female
Male

GRAPH 5

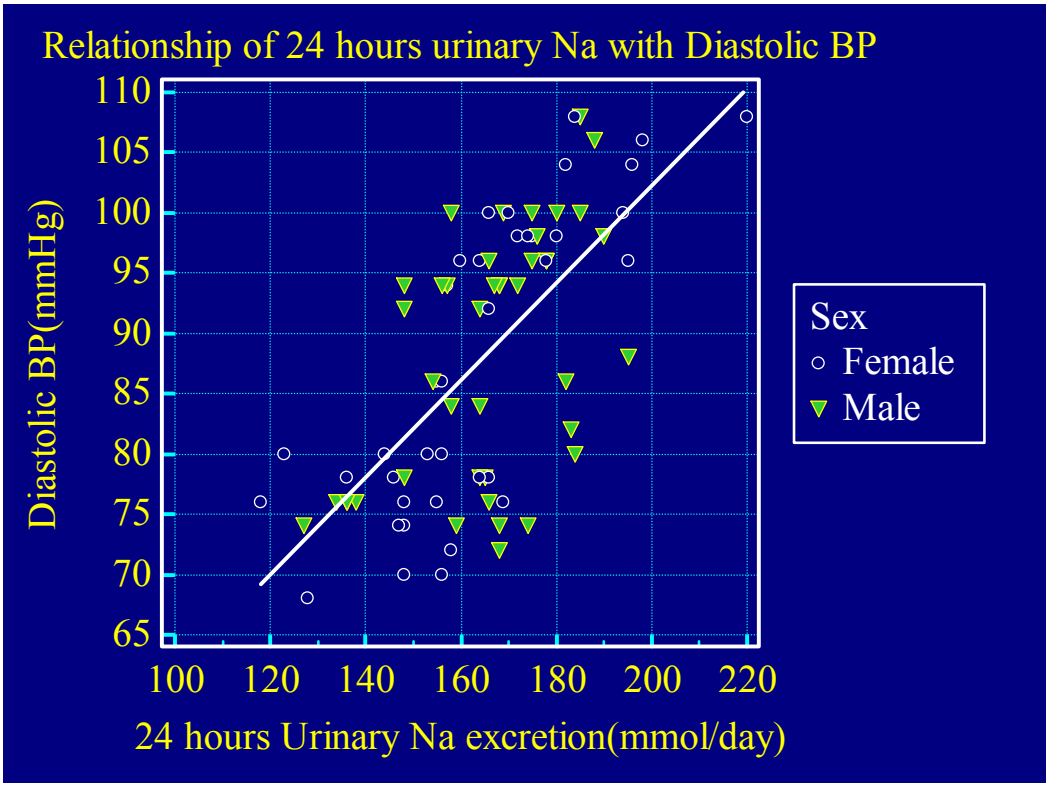

Relationship of 24 hours urinary Na with Diastolic BP
Diastolic BP(mmHg)
110
105
100
95
90
85
80
75
70
65
100
120
140
160
180
200
220
24 hours Urinary Na excretion(mmol/day)
Sex
Female
Male

TABLE 12

Relationship of 24 hours urinary sodium and potassium excretion with severity of systolic hypertension

Group	Severity of systolic hypertension				P value
	Mild		Moderate toSevere		
	No	Mean±S.D	No	Mean±S.D	
Urinary sodium excretion	11	163.636 ± 13.002	29	178.689 ±13.039	0.002
Urinary potassium excretion	11	49.727 ± 6.247	29	54.038 ±7.476	0.098

Of the forty subjects in the hypertensive group ,11 subjects had mild hypertension and 29 subjects had moderate to severe hypertension.

In the group with mild hypertension,the average 24 hour urinary sodium excretion was 163.636 with a standard deviation of 13.002 .

In the group with moderate to severe hypertension ,the average 24 hour urinary sodium excretion was 178.689 with a standard deviation of 13.039.

P value was 0.002 which was significant.

The mean 24 hour urinary sodium excretion was higher in patients with moderate to severe hypertension when compared to subjects with mild hypertension which was statistically significant.

The average 24 hour urinary potassium excretion in patients with mild hypertension was 49.727 with a standard deviation of 6.247.

The average 24 hour urinary potassium excretion in patients with moderate to severe hypertension was 54.038 with a standard deviation of 7.476.P value was 0.098 which was statistically insignificant.

TABLE 13

Relationship of 24 hour urinary sodium and potassium excretion with severity of diastolic hypertension

Group	Severity of diastolic hypertension				P value
	Mild		Moderate to Severe		
	No	Mean±S.D	No	Mean ± S.D	
Urinary sodium excretion	25	169.28 ± 11.433	15	183.33 ± 15.282	0.002
Urinary potassium excretion	25	51.920 ± 7.729	15	54.400 ± 6.609	0.307

The average 24 hour urinary sodium excretion in patients with mild diastolic hypertension was 169.28 with a standard deviation of 11.433.

The average 24 hour urinary sodium excretion in patients with moderate to severediastolic hypertension was 183.33 with a standard deviation of 15.282.

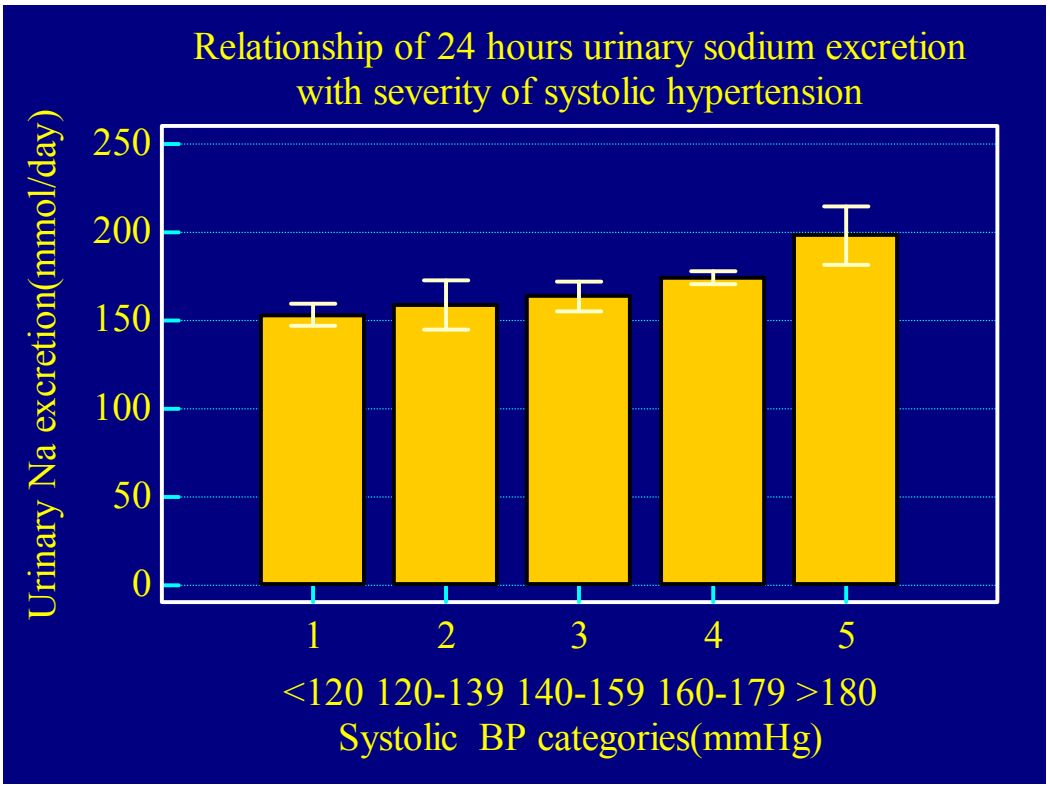
P value was 0.002 which was significant.This suggests that there was significant increase in 24 hour urinary sodium excretion with increasing severity of diastolic hypertension.

The average 24 hour urinary potassium excretion in patients with mild diastolic hypertension was 51.920 with a standard deviation of 7.729.

The average 24 hour urinary potassium excretion in patients with moderate to severe diastolic hypertension was 54.400 with a standard deviation of 6.609.

P value was 0.307 which was not significant. So, there was no significant difference in the 24 hour urinary potassium excretion with increasing severity of diastolic hypertension.

GRAPH 6


Relationship of 24 hours urinary sodium excretion
with severity of systolic hypertension
Urinary Na excretion(mmol/day)
250
200
150
100
50
0
1
2
3
4
5
<120 120-139 140-159 160-179 >180
Systolic BP categories(mmHg)

GRAPH 7

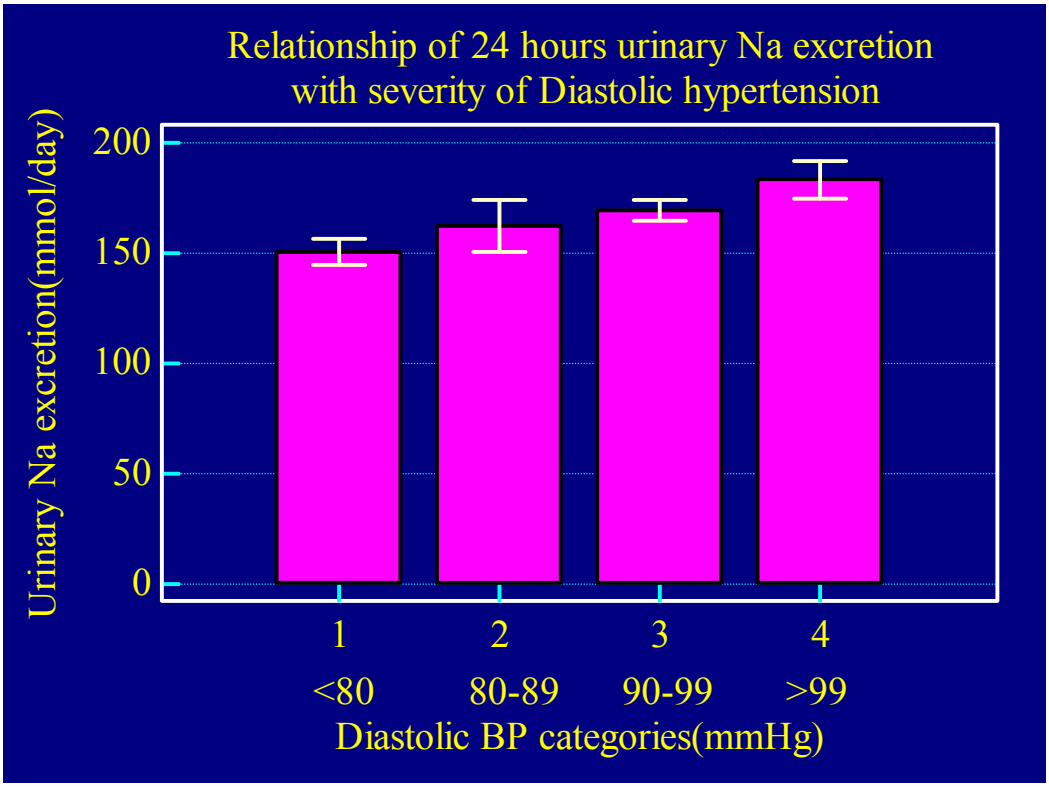

Relationship of 24 hours urinary Na excretion
with severity of Diastolic hypertension
Urinary Na excretion(mmol/day)
200
150
100
50
0
1
2
3
4
<80
80-89
90-99
>99
Diastolic BP categories(mmHg)

TABLE 14

24 hour urinary sodium excretion by age and sex in the study group

AGE GROUP	NO	MEAN	S.D
20 - 35	7	158.00	26.134
36 - 50	40	161.20	15.162
51 - 70	33	169.85	20.358
SEX	NO	MEAN	S.D
Males	42	166.57	16.359
Females	38	163.29	21.388

The mean 24 hour urinary sodium excretion in 20 – 35 age group was 158 ± 26.134,36 – 50 age group was 161.20 ± 15.162, and 51 – 70 age group was 169.85 ± 20.36.

The mean 24 hour urinary sodium excretion in the entire study group increased significantly with advancing age which shows the influence of age on urinary sodium excretion.

The mean 24 hour urinary sodium excretion in the entire study group was significantly higher in males (166.57 ± 16.359) when compared to females (163.29 ± 21.388).

TABLE 15

24 hour urinary sodium excretion in relation to gender in each age group in the study population

AGE GROUP	GENDER	NO	MEAN
20 – 35	Males	3	167
	Females	4	151.25
36 – 50	Males	24	162.42
	Females	16	159.38
51 - 70	Males	15	170.33
	Females	18	169.44

In age group of 20 – 35,the mean 24hour urinary sodium excretion in males was 167 and females was 151.25.

In age group of 36 – 50, the mean 24hour urinary sodium excretion in males was 162.42 and females was 159.38.

In age group of 51 – 70, the mean 24hour urinary sodium excretion in males was 170.33 and females was 169.44.

In all the age groups,mean 24 hour urinary sodium excretion was significantly higher in males as compared to females.

TABLE 16

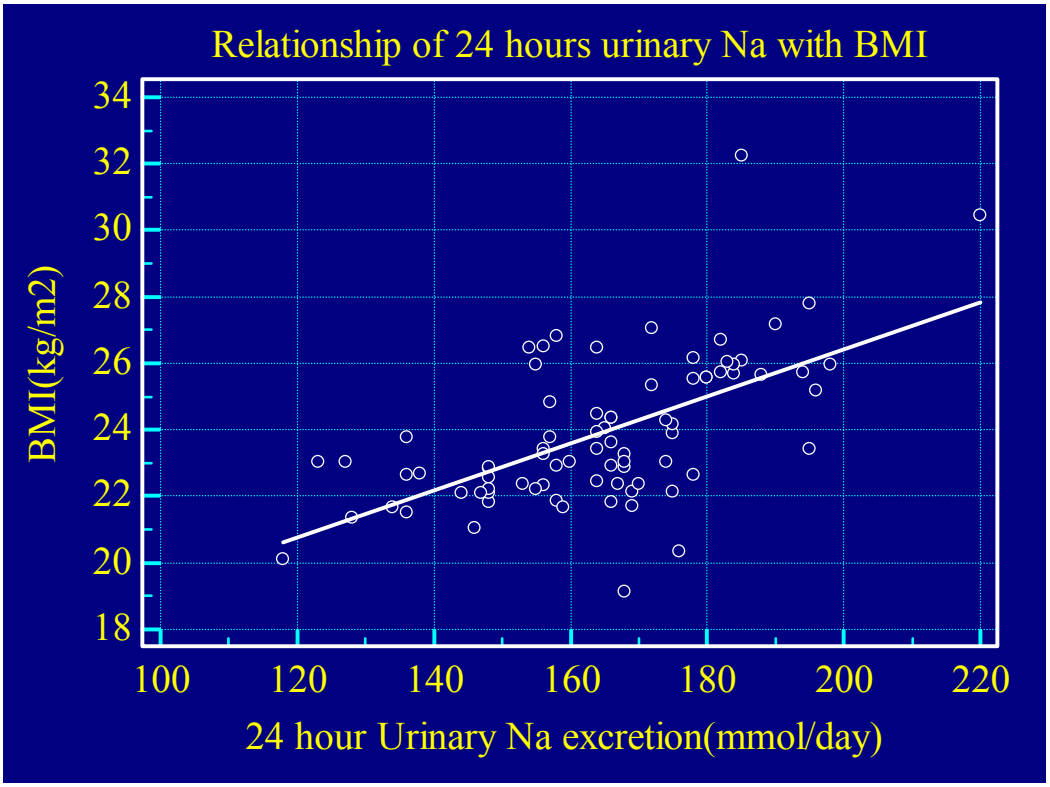
Relationship of BMI with 24 hours urinary sodium , potassium excretion in hypertensives and normotensives

Group	BODY MASS INDEX				P value
	BMI < 25		BMI > 25		
HYPERTENSIVES	NO	MEAN	NO	MEAN	
Urinary sodium	24	166.67	16	186.38	< 0.001
Urinary potassium	24	51.58	16	54.75	0.185
NORMOTENSIVES	NO	MEAN	NO	MEAN	
Urinary sodium	31	149.87	9	170.11	0.001
Urinary potassium	31	55.87	9	51.67	0.157

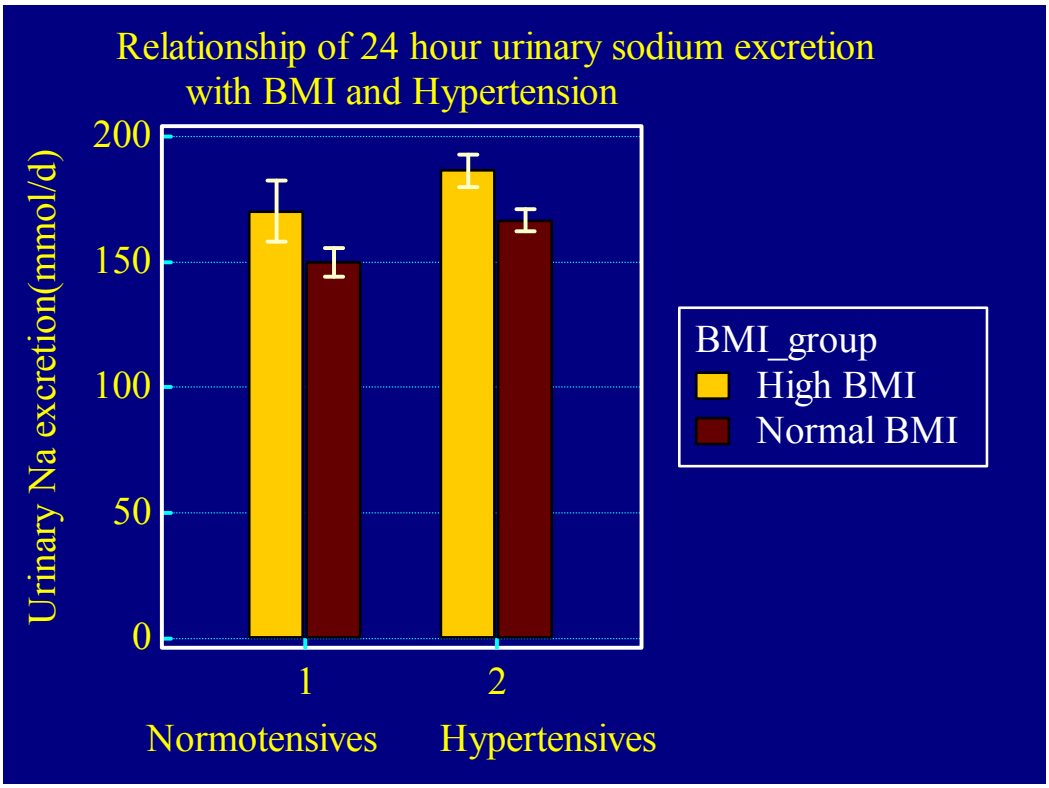
In hypertensive patients , the mean 24 hour urinary sodium excretion in subjects with normal BMI was 166.67 while the mean 24 hour urinary sodium excretion in subjects with high BMI was 186.38. P value was less than 0.001 which was significant.

In normotensive subjects,the mean 24 hour urinary sodium excretion in subjects with normal BMI was 149.87 while the mean 24 hour urinary sodium excretion in subjects with high BMI was 170.11. P value was 0.001 which was significant.

GRAPH 8


Relationship of 24 hours urinary Na with BMI
BMI(kg/m2)
34
32
30
28
26
24
22
20
18
100
120
140
160
180
200
220
24 hour Urinary Na excretion(mmol/day)

GRAPH 9


Relationship of 24 hour urinary sodium excretion
with BMI and Hypertension
Urinary Na excretion(mmol/d)
200
150
100
50
0
1
2
Normotensives
Hypertensives
BMI_group
High BMI
Normal BMI

In hypertensive patients , the average 24 hour urinary potassium excretion in subjects with normal BMI was 51.58 while the average 24 hour urinary potassium excretion in subjects with high BMI was 54.75. P value was 0.185 which was not significant.

In normotensive subjects ,the average 24 hour urinary potassium excretion in subjects with normal BMI was 55.87 while the average 24 hour urinary potassium excretion in subjects with high BMI was 51.67. P value was 0.157 which was not significant.

Both the hypertensive and normotensive group showed a significant increase in 24 hour urinary sodium excretion in subjects with high BMI when compared to normal BMI.

There was no significant difference in 24 hour urinary potassium excretion between normal and high BMI subjects in both hypertensive and normotensive group.

This shows that BMI has significant influence on 24 hour urinary sodium excretion irrespective of blood pressure level.

TABLE 17

Correlation between blood pressure and 24 hour urinary sodium excretion in hypertensivesafter adjusting for confounding factors

Hypertensives	Systolic BP		Diastolic BP	
	r	p	r	p
Urinary sodium	0.6372	<0.0001	0.5310	0.0009
Urinary potassium	-0.3547	0.0338	0.1001	0.5615

In hypertensive patients,the partial correlation co-efficient ‘r’ was 0.6372 and p value was less than 0.0001 for correlation between 24hour urinary sodium excretion and systolic blood pressure, which was statistically significant.

The partial correlation co-efficient ‘r’ was 0.5310 and p value was 0.0009 for correlation between 24 hour urinary sodium excretion and diastolic blood pressure ,which was statistically significant.

There was significant correlation between 24 hour urinary K^+excretion (r = -0.3547,p = 0.0338) and systolic blood pressure while there was no significant correlation between diastolic blood pressure and 24 hour urinary K^+ excretion(r=0.1001,p=0.561) in hypertensive patients.

DISCUSSION

Hypertension is one of the world's great public health problems and leading cause of death. [51] Essential hypertension accounts for about 90% of all hypertensive patients. [52]

Multiple factors are responsible for the development of hypertension.One of the causal factors proposed is high sodium intake along with low potassium intake and excretion. [2]

Our present study was conducted to test this causal relationship between sodium,potassium intake and hypertension by measuring 24 hour urinary sodium and potassium excretion.

In our study, the mean 24 hour urinary sodium excretion was significantly elevated in hypertensive group when compared to normotensive group which was statistically significant (p value <0.0001). Our observation was similar to that recorded in the Intersaltstudy. [3] Many other studies have shown excessive 24 hour urinary sodium excretion in hypertensive patients. [53] [54] [4]

Excessive 24 hour urinary sodium excretion observed in hypertensive patients in our study could probably be responsible for the development of hypertension which was proved in various other

studies. [2] [53] [55] This was further supported by the fact that low salt intake reduces hypertension and low prevalence of hypertension in population with low salt intake. [55] [56] [57]

In our study,the average 24 hour urinary potassium excretion was lower in both hypertensive and normotensive groups probably due to low potassium intake.Menealy and Belarbee in 1976 found that low potassium intake contributes to hypertension. [2] Various other studies have also confirmed that low potassium intake leads to hypertension , independent of sodium excretion. [58] [59]

Excessive 24 hour urinary sodium excretion and lower 24 hour urinary potassium excretion in our hypertensive group indicates that both high sodium intake and low potassium intake additively contribute to the rise in blood pressure.Further urinary Na^+/K^+ molar ratio was higher in hypertensive groups when compared to normotensives which was due to increased urinary sodium excretion in hypertensive group as shown in various other studies. [4]

Our study observed significant influence of 24 hour urinary sodium excretion on the severity of hypertension.The mean 24 hour urinary sodium excretion was significantly higher in patients with severe hypertension as compared to mild to moderate hypertension which was

statistically significant (p value = 0.002).There was no association between 24 hour urinary potassium excretion and severity of hypertension.Similar observations were also recorded by RA Jan et al in 2006. [4]

In our study, several confounding variables such as age, gender,BMI and serum cholesterol were present which could have contributed to hypertension apart from the impact of 24 hour urinary sodium and potassium excretion.

Age was the first factor to be independently associated with blood pressure .Age influences the capacity of kidneys to conserve sodium. [60] Advancing age leads to both a decline in glomerular filtration rate and an increased incidence of renal disease [61] which contributes to increased urinary sodium excretion in elderly people. [62] This was proved by our study which showed a significant increase in 24 hour urinary sodium excretion with advancing age.(Table 14)

Simpson et al in 1978 found that mean 24 hour urinary sodium excretion at all ages was significantly higher in males when compared to females. [63] Similar results were obtained in our study which showed a higher 24 hour urinary sodium excretion in males as compared to females

at all age groups.(Table 15)This could be probably because of their overall higher food intake and differences in food habits. [64] [65] [66] [67]

Our study demonstrated a significant impact of BMI on 24 hour urinary sodium excretion. In both hypertensive and normotensive groups,24 hour urinary sodium excretion increased significantly with high BMI.There was no association between urinary potassium excretion and BMI in either group.(Table 16)

INTERSALT STUDY has shown significant and independent relationship of BMI with hypertension in individual subjects [3] which was proved in our study . Simpson et al in 1978 [63] also proved similar relationship of BMI with urinary sodium excretion and hypertension as observed in our study.

The OLIVETTI HEART STUDY showed that physiological regulation of sodium reabsorption at the proximal tubule was maintained in normal weight individuals ; higher the sodium intake,the lower its reabsorption at the proximal tubule.In contrast, this physiological regulation was found to be altered in overweight/obese individuals , being independent of the total amount of sodium ingested.This leads to increased urinary sodium excretion in high BMI subjects as observed in our study.

In our study,the next factor independently associated with blood pressure was serum cholesterol ,which has been proved beyond doubt as an independent risk factor for hypertension. [68]

The relationship of 24 hour urinary sodium and potassium excretion with blood pressure was analysed again after controlling for the confounding factors.

In hypertensive patients, systolic blood pressure correlated significantly with 24 hour urinary sodium excretion($r = 0.64$, $p < 0.0001$) and 24 hour urinary potassium excretion ($r = -0.35$, $p = 0.033$) even after adjustment for age, gender,BMI,serum cholesterol.

In normotensive controls, systolic blood pressure does not correlate with 24 hour urinary sodium excretion ($r = 0.02$, $p = 0.92$) and potassium excretion ($r = 0.19$, $p = 0.25$).

In hypertensive patients ,diastolic blood pressure correlated with urinary Na^+ excretion($r = 0.53$,$p = 0.0009$) but did not correlate with urinary K^+ excretion($r = 0.10$, $p = 0.56$) after adjustment for age,sex,BMI and serum cholesterol.Similar observation was made by B.M.Y.Cheung et al in Chinese population. [47] In normotensive controls, diastolic blood pressure did not correlate with urinary Na^+ excretion ($r = 0.22$, $p = 0.19$).

SUMMARY

Forty hypertensive patients and equal number of age and sex matched controls were taken up for studying the relationship between 24 hour urinary sodium and potassium excretion with blood pressure in hypertensive and normotensive subjects at Government Rajaji Hospital, Madurai.

In hypertensive group , there was significantly elevated 24 hour urinary sodium excretion and Na^+/ K^+ molar ratio whereas there was lower 24 hour urinary potassium excretion.24 hour urinary sodium excretion also correlated with severity of hypertension.

Age , gender, BMI and serum cholesterol had significant influence on 24 hour urinary sodium excretion.

Even after adjustment for age, gender,BMI and serum cholesterol, 24 hour urinary sodium excretion significantly correlated with both systolic and diastolic blood pressure in hypertensive patients.

24 hour urinary potassium excretion correlated only with systolic blood pressure after adjustment for age,gender,BMI and serum cholesterol.

CONCLUSION

1.Significantly elevated 24 hour urinary sodium excretion and low potassium excretion in our study suggests that both very high sodium intake and low potassium intake play a significant role individually as well as additively in the development or perpetuation of hypertension.

2.BMI and serum cholesterol were strongly ,positively and independently associated with blood pressure in individual subjects.

3.Age and sex have significant influence on urinary sodium excretion and blood pressure.

The final conclusion from our study is that longterm reduction in salt intake would significantly reduce the prevalence of hypertension and thereby decrease associated morbidity and mortality due to cardiovascular disease and stroke.

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ABBREVIATIONS

RAAS	-	Renin – angiotensin – aldosterone system
A II	-	Angiotensin II
RIHP	-	Renal interstitial hydrostatic pressure
GFR	-	Glomerular filtration rate
FSA	-	Filtration surface area
HT	-	Hypertension
AME	-	Apparent mineralocorticoid excess
Na^+	-	Sodium
K^+	-	Potassium
RKKS	-	Renin – kallikrein – kinin system
GRA	-	Glucocorticoid Remediable Aldosteronism
SVR	-	Systemic vascular resistance
RSNA	-	Renal sympathetic nerve activity

PROFORMA

NAME :

AGE :

SEX :

OCCUPATION :

ADDRESS :

SYMPTOMS :

Head ache	Chest pain	Weakness	Swelling over legs
Dizziness	Breathlessness	Weight gain	Excessive sweating
Fatigue	Visual problems	Tremors	Decreasedurineoutput
Palpitation	Abdominal mass	Facial puffiness	Heat/cold intolerance

PAST ILLNESS:

Hypertension – duration,levels of elevated blood pressure

Diabetes

Coronary artery Disease /Cerebrovascular accident

FAMILY HISTORY :

Hypertension

Diabetes

Coronary artery disease/Cerebrovascular accident

Renal disease

PERSONAL HISTORY :

Smoking

Alcohol intake

DRUG HISTORY :

All prescribed and over the counter medications

GENERAL EXAMINATION

ANTHROPOMETRY :

Height :

Weight :

BMI :

Anaemia/Jaundice/Cyanosis/Clubbing/Facial puffiness/Pedal edema

Arcus senilis/Xanthelesma/Xanthomas

Thyroid swelling

Fundus examination

VITALS

Pulse :

BP :

JVP :

SYSTEMIC EXAMINATION

CVS :

RS :

ABDOMEN :

CNS :

INVESTIGATIONS

Urine – albumin, sugar, deposits

Blood – sugar , urea, creatinine

Serum – sodium , potassium

Lipid profile – TGL, LDL, HDL, Cholesterol

Serum – calcium, phosphorus

Serum – uric acid

24 hours urinary excretion of sodium and potassium

Thyroid profile

Chest Xray PA view

Electrocardiogram

Echocardiography

USG Abdomen and pelvis

Patients were evaluated on the basis of proforma of above guidelines.

MASTER CHART – CASES : HYPERTENSIVE SUBJECTS

S.No	Age	Sex	BMI	Serum Sodium	Serum Potassium	Serum Calcium	Serum Phosphorus	Serum Cholesterol	Blood Sugar	Blood Urea	Blood Creatinine	Serum Uric acid	Urinary Sodium	Urinary Potassium	Systolic Blood pressure	Diastolic Blood pressure
1	35	Male	25.56	142	3.5	9.4	3.6	198	102	24	0.8	5.6	180	56	178	100
2	42	Male	25.53	143	3.6	10	3.8	200	98	26	0.9	5.7	178	46	164	96
3	45	Male	22.82	139	3.8	9.3	3.5	194	97	32	0.9	5.8	148	60	150	94
4	45	Male	21.88	137	3.9	9.4	3.7	188	110	34	0.5	6.2	158	62	168	100
5	68	Female	25.96	146	3.6	10.2	4.1	198	98	36	1	6.4	198	58	180	106
6	45	Female	23.89	142	3.7	9	4.2	186	98	42	0.9	6.5	175	43	146	98
7	52	Male	26.14	142	4.1	9.4	4	220	96	40	0.8	5.5	178	55	166	96
8	44	Male	27.06	143	3.5	9.2	3.9	210	95	25	0.7	5.4	172	60	162	94
9	46	Male	27.16	145	3.8	10.2	3.5	200	104	35	1.5	5.3	190	46	158	98
10	36	Male	19.15	135	3.7	9.1	3.7	179	96	41	1.3	5.2	168	62	164	94
11	50	Female	22.66	138	3.9	9.5	3.8	186	97	44	0.5	5.5	178	50	156	96
12	67	Female	30.46	144	4.2	9.1	3.5	245	98	38	1.5	5.4	220	54	180	108
13	55	Male	22.46	143	3.8	9.2	3.5	186	115	36	0.6	6.2	164	69	162	92
14	55	Female	24.81	136	3.7	10	4	188	120	23	0.8	5.6	157	44	154	94
15	57	Female	24.47	134	4.3	9.3	3.6	194	98	43	0.7	6.3	164	56	158	96
16	66	Male	23.28	135	3.6	9.3	3.7	184	96	41	0.9	5.5	168	41	162	94
17	57	Female	23.63	134	3.5	9.6	3.8	188	94	26	1.5	5.4	166	58	166	92
18	40	Male	23.79	136	3.8	11	3.9	186	97	22	1.3	5.6	157	43	156	94
19	46	Male	22.14	145	4.5	10.5	3.5	179	113	28	1.6	5.5	169	46	168	100
20	42	Male	22.35	139	3.5	9.5	3.5	177	120	29	1.2	5.4	156	59	156	94

21	38	Male	24.37	137	4.5	9.4	4.1	183	115	36	0.8	5.8	166	47	166	96
22	49	Male	22.58	146	3.8	9.4	4.4	186	130	32	0.7	5.7	148	46	146	92
23	49	Male	32.25	143	3.7	9.2	3.8	240	97	33	0.9	6.8	185	65	178	108
24	53	Female	23.43	134	3.6	9.6	3.7	192	98	38	0.8	5.8	195	43	174	96
25	36	Male	22.36	142	4.4	9.1	3.4	186	97	44	0.8	6.4	167	48	148	94
26	55	Female	23.04	137	3.9	9	3.4	194	112	46	1.3	6.6	160	52	154	96
27	63	Female	25.32	144	4.8	10.4	3.6	197	115	45	0.9	6.8	172	56	166	98
28	60	Female	25.74	145	3.5	10.2	3.8	198	98	32	0.9	5.4	182	44	176	104
29	46	Female	21.81	134	3.8	9.3	4.1	175	97	43	1	5.8	166	48	172	100
30	55	Female	25.2	143	5	9.4	4.5	197	96	40	1.2	5.9	196	52	180	104
31	55	Male	25.64	146	3.6	9.3	4.5	194	95	41	1	6.2	188	62	178	106
32	65	Male	20.33	136	3.8	10.1	3.8	174	104	39	1	5.8	176	50	168	98
33	50	Male	24.16	145	3.7	9.4	3.5	192	112	38	0.9	5.8	175	65	176	96
34	68	Male	22.14	138	3.9	9.4	3.6	182	99	37	1	5.7	175	52	168	100
35	64	Female	25.57	144	4	9.7	3.5	197	96	37	0.8	5.6	180	53	176	98
36	30	Female	25.7	141	3.5	9.2	3.6	198	114	38	0.9	6.4	184	50	180	108
37	38	Female	22.36	137	4.1	9	3.6	178	130	42	0.8	7.1	170	48	166	100
38	45	Female	23.05	139	3.8	9	3.4	184	112	44	1.2	7.5	174	46	172	98
39	25	Male	26.09	143	3.9	10.3	3.5	196	98	40	0.9	6.8	185	63	178	100
40	52	Female	25.74	145	4.8	11	3.6	191	99	38	1.5	6.4	194	56	186	100

MASTER CHART – CONTROLS: NORMOTENSIVE SUBJECTS

41	45	Male	24.28	135	3.6	9	3.5	184	120	33	0.9	6.4	174	58	118	74
42	44	Male	22.89	141	3.4	8.5	3.6	174	112	32	0.8	6.2	168	65	116	72
43	52	Male	25.95	140	4.2	9.6	3.5	193	103	30	1.3	5.8	184	48	120	80
44	44	Female	21.69	139	4.6	8.7	3.5	176	98	28	0.9	5.6	169	63	116	76
45	63	Male	24.06	146	3.5	8.8	3.4	182	96	26	1	5.4	165	67	114	78
46	37	Female	21.81	138	3.7	8.9	3.4	195	95	25	1.2	5.6	148	46	110	70
47	54	Male	24.37	135	3.9	9.3	3.8	174	113	34	1	5.5	166	58	114	76
48	38	Female	22.92	138	3.6	9.5	3.7	178	104	36	0.5	7.2	158	58	116	72
49	48	Male	23.42	142	3.8	10	4	181	95	38	1.5	6.5	164	48	118	78
50	41	Female	22.92	140	3.6	11	4.2	178	96	25	0.8	8	166	64	116	78
51	48	Female	22.22	138	3.5	9	4.2	178	104	28	0.7	5	155	52	112	76
52	64	Male	23.05	137	4.2	8.8	3.6	184	110	29	1.2	6.4	168	68	116	74
53	65	Male	22.66	141	3.6	8.9	3.5	174	104	34	0.9	6.2	136	56	112	76
54	57	Male	26.02	136	4.3	9.1	3.6	196	99	36	1.5	5.6	183	48	120	82
55	58	Female	22.08	143	3.5	9.3	3.6	184	103	38	0.9	5.8	148	58	110	74
56	43	Male	22.68	137	3.6	9.5	3.7	179	114	44	0.8	5.5	138	44	112	76
57	58	Female	21.34	136	3.7	9.7	3.8	198	103	42	0.9	5.7	128	68	100	68
58	42	Female	21.05	137	3.8	9.8	3.5	175	98	40	0.7	5.6	146	45	118	78
59	40	Male	21.65	138	3.5	8.7	3.6	173	96	36	1.3	5.8	134	48	114	76
60	63	Male	26.72	135	3.5	8.9	3.6	188	98	38	1.4	6.2	182	63	124	86

61	34	Female	20.09	136	3.8	8.9	3.4	165	104	46	0.9	5.6	118	49	110	76
62	46	Male	22.89	138	3.7	9.2	3.5	192	110	48	0.8	4.8	148	57	114	78
63	58	Female	25.95	141	3.8	9.4	3.6	196	98	47	0.5	5.7	155	67	120	86
64	48	Male	27.79	138	3.6	9.5	3.6	194	98	40	0.5	5.6	195	46	116	88
65	47	Female	22.36	139	4.4	10.4	3.4	180	110	36	0.8	5.9	153	49	126	80
66	45	Female	23.94	138	4.3	9.8	3.8	178	97	35	0.6	6.2	164	53	118	78
67	48	Male	26.81	143	3.7	11	4.2	196	98	34	0.6	4.4	158	47	122	84
68	38	Female	22.22	139	3.8	9.3	4.5	168	98	36	1	5.8	148	59	112	76
69	48	Male	21.65	135	3.9	9.5	4.1	165	99	44	1.2	6.4	159	46	100	74
70	54	Female	23.05	136	3.6	10.1	3.6	170	104	26	0.5	5.8	123	54	120	80
71	45	Male	26.45	145	3.7	11	3.5	191	103	42	1	3.6	164	55	126	84
72	36	Female	22.08	138	3.5	9	3.6	168	112	40	0.9	5.6	144	57	118	80
73	31	Male	23.79	137	3.8	9.4	3.8	198	106	23	0.8	5.8	136	56	114	76
74	36	Male	23.05	141	3.7	9.6	3.5	188	105	24	0.9	6.2	127	64	108	74
75	34	Female	23.42	135	3.6	9.5	3.4	162	104	25	1.3	5.5	156	57	110	70
76	63	Female	26.51	136	3.5	9.6	3.5	210	105	20	0.8	5.6	156	47	124	86
77	62	Male	26.47	138	3.9	9.4	4.2	230	98	41	0.9	5.8	154	44	128	86
78	46	Female	21.52	136	3.8	9.5	3.6	176	97	42	0.8	6.2	136	48	116	78
79	20	Female	22.09	135	4	9.2	3.6	175	96	36	0.7	5.5	147	69	114	74
80	54	Female	23.28	135	4.2	9.3	3.5	180	95	22	0.9	5	156	48	118	80

Ref. No. 3104/E4/3/2012

Govt.Rajaji Hospital,Madurai.20.
Dated: .03.2012

Institutional Review Board / Independent Ethics Committee.
Dr. A. Edwin Joe, M.D (FM), BL.,
Dean, Madurai Medical College & 2521021 (Secy)
Govt Rajaji Hospital, Madurai 625020.
Convenor
grhethicssecy @gmail.com.

Sub: Establishment-Govt. Rajaji Hospital, aMadurai-20-
Ethics committee-Meeting Agenda-communicated-regarding.

The Ethics Committee meeting of the Govt. Rajaji Hospital, Madurai was held at 11.00 Am to 1.00Pm on 29.03.2012 at the Dean Chamber, Govt. Rajaji Hospital, Madurai. The following members of the committee have been attended the meeting.

1. Dr.N.Vijayasankaran,M.ch(Uro.) 094-430-58793 0452-2584397	Sr.Consultant Urologist Madurai Kidney Centre, Sivagangai Road,Madurai	Chairman
2. Dr.P.K. Muthu Kumarasamy, M.D., 9843050911	Professor & H.O.D of Medical, Oncology(Retired)	Member Secretary
3. Dr.T.Meena,MD 094-437-74875	Professor of Physiology, Madurai Medical College	Member
4. Dr. S. Thamilarasi, M.D (Pharmacol)	Professor of pharmacology	
5. Dr.Moses K.Daniel MD(Gen.Medicine) 098-421-56066	Professor of Medicine Madurai Medical College	Member
6. Dr.M.Gobinath,MS(Gen.Surgery)	Professor of Surgery Madurai Medical College	Member
7. Dr.S. Dilshadh, MD(O&G) 9894053516	Professor of OP&Gyn Madurai Medical College	Member
8. Dr.S.Vadivel Murugan., M.D, 097-871-50040	Professor of Medicine Madurai Medical College	Member
9. Shri.M.Sridher,B.sc.B.L. 099-949-07400	Advocate, 2, Deputy collectors colony 4th street KK Nagar, Madurai-20.	Member
10. Shri.O.B.D.Bharat,B.sc., 094-437-14162	Businessman Plot No.588, K.K.Nagar,Madurai.20.	Member
11.Shri. S.sivakumar,M.A(Social) Mphil 093-444-84990	Sociologist, Plot No.51 F.F, K.K Nagar, Madurai.	Member

Following Projects were approved by the committee

Sl. No	Name of P.G.	Course	Name of the Project	Remarks
1.	Indumathy. C	PG, M.D (genl Med	24-hour urinary Na and K excretion and blood pressure	Approved

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain Confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution to Government.
2. She/He should inform the institution Ethical Committee in case of any change of study procedure site and investigation or guide.
3. She/He should not deviate for the area of the work for which applied for Ethical clearance. She/He should inform the IEC immediately, in case of any adverse events pr Serious adverse reactions.
4. She/he should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and apply for if any Extension of time is required She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the Ethical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the word or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

DEAN

To
All the above members and Head of the Departments concerned.
All the Applicants.

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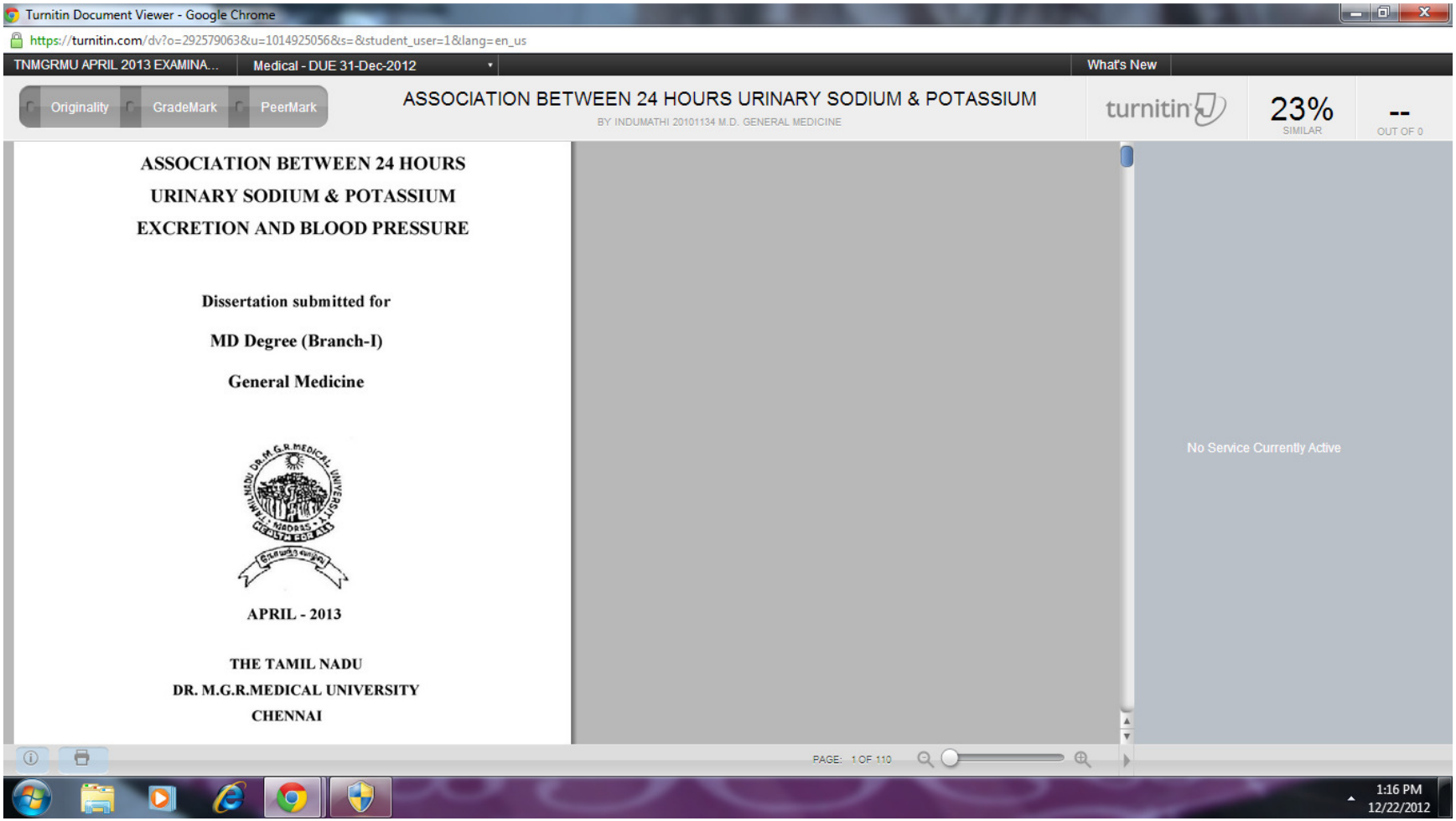

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ASSOCIATION BETWEEN 24 HOURS URINARY SODIUM & POTASSIUM EXCRETION AND BLOOD PRESSURE Dissertation submitted for MD Degree (Branch-I) General Medicine APRIL - 2013 THE TAMIL NADU DR. M.G.R.MEDICAL UNIVERSITY CHENNAI CERTIFICATE This is to certify that this dissertation titled “ASSOCIATION BETWEEN 24 HOURS URINARY SODIUM & POTASSIUM EXCRETION AND BLOOD PRESSURE” submitted by DR. C.INDUMATHI to the faculty of General Medicine, The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree Branch I (General Medicine) is a bonafide research work carried out by her under our direct supervision and guidance. Dr.G.Bagialakshmi MD., Associate...